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FIRST AID FOR THE®
Pediatrics Clerkship

Fourth Edition

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Contents

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How to Succeed in the Pediatrics Clerkship

Introduction

This clinical study aid was designed in the tradition of the First Aid series of books. You will find that rather than simply preparing you for success on the clerkship exam, this resource will also help guide you in the clinical diagnosis and treatment of many of the problems seen by pediatricians. The content of the book is based on the objectives for medical students laid out by the Council on Medical Student Education in Pediatrics (COMSEP). Each of the chapters contains the major topics central to the practice of pediatrics and has been specifically designed for the third-year medical student learning level.

The content of the text is organized in the format similar to other texts in the First Aid series. Topics are listed by bold headings, and the "meat" of the topic provides essential information. The outside margins contain mnemonics, diagrams, summary or warning statements, and tips. Tips are categorized into typical scenarios **Typical Scenario**, exam tips ♟, and ward tips ✋.

The pediatric clerkship is unique among all the medical school rotations. Even if you are sure you do not want to be a pediatrician, it can be a very fun and rewarding experience. There are three key components to the rotation: (1) what to do on the wards, (2) what to do on outpatient, and (3) how to study for the exam.

On the Wards . . .

Be on time. Most ward teams begin rounding around 7 AM. If you are expected to "pre-round," you should give yourself at least 15 minutes per patient that you are following to see the patient, look up any tests, and learn about the events that occurred overnight. Like all working professionals, you will face occasional obstacles to punctuality, but make sure this is occasional. When you first start a rotation, try to show up at least an extra 15 minutes early until you get the routine figured out. There may be "table rounds" followed by walking rounds, but the emphasis is patient and family-centered.

Family-centered rounds is a model of communicating and learning between the patient, family, medical professionals, and students on an academic, inpatient ward setting.

Find a way to keep your patient information organized and handy. By this rotation, you may have figured out the best way for you to track your patients including a focused physical, medications, labs, test results, and daily progress. If not, ask around—other medical students or your interns can show you what works for them and may even make a copy for you of the template they use. We suggest index cards, a notebook, or a page-long template for each patient kept on a clipboard.

Dress in a professional manner. Even if the resident wears scrubs and the attending wears stiletto heels, you must dress in a professional, conservative manner. It would be appropriate to ask your resident what would be

suitable for you to wear (it may not need to be a full suit and tie or the female equivalent). Wear a short white coat over your clothes unless discouraged.

> **Men** should wear long pants, with cuffs covering the ankle, a long-sleeved, collared shirt, and a tie—no jeans, no sneakers, no short-sleeved shirts, no flip-flops.
> **Women** should wear long pants or a knee-length skirt and blouse or dressy sweater—no jeans, sneakers, heels greater than 1½ inches, or open-toed shoes.
> **Both men and women** may wear scrubs during overnight call. Do not make this your uniform.

Act in a pleasant manner. Inpatient rotations can be difficult, stressful, and tiring. Smooth out your experience by being nice to be around. Introduce yourself to the team you will be working with, including the attendings, the residents, the nurses, and the ancillary staff. Smile a lot and learn everyone's name. If you do not understand or disagree with a treatment plan or diagnosis, do not "challenge." Instead, say "I'm sorry, I don't quite understand, could you please explain . . . ." Be empathetic toward patients.

Be aware of the hierarchy. The way in which this will affect you will vary from hospital to hospital and team to team, but it is always present to some degree. In general, address your questions regarding ward functioning to interns or residents. Address your medical questions to residents, your senior, or the attending. Make an effort to be somewhat informed on your subject prior to asking attendings medical questions.

Address patients and staff in a respectful way. Address your pediatric patients by first name. Address their parents as Sir, Ma'am, or Mr., Mrs., or Miss. Do not address parents as "honey," "sweetie," and the like. Although you may feel these names are friendly, parents will think you have forgotten their name, that you are being inappropriately familiar, or both. Address all physicians as "doctor" unless told otherwise. Nurses, technicians, and other staff are indispensable and can teach you a lot. Please treat them respectfully.

Take responsibility for your patients. Know everything there is to know about your patients—their history, test results, details about their medical problem, and prognosis. Keep your intern or resident informed of new developments that he or she might not be aware of, and ask for any updates of which you might not be aware. Assist the team in developing a plan, and speak to radiology, consultants, and family. Never give bad news to patients or family members without the assistance of your supervising resident or attending. **Respect patients' rights.**

- All patients have the right to have their personal medical information kept private. This means do not discuss the patient's information with family members without that patient's consent, and do not discuss any patient in hallways, elevators, or cafeterias.
- All patients have the right to refuse treatment. This means they can refuse treatment by a specific individual (e.g., you, the medical student) or of a specific type (e.g., no nasogastric tube [NGT]). Patients can even refuse lifesaving treatment. The only exceptions to this rule are patients who are deemed to not have the capacity to make decisions or understand situations, in which case a health care proxy should be sought, and patients who are suicidal or homicidal.
- All patients should be informed of the right to seek advanced directives on admission (particularly DNR/DNI orders). Often, this is done in a booklet

by the admissions staff. If your patient is chronically ill or has a life-threatening illness, address the subject of advanced directives. The most effective way to handle this is to address this issue with every patient. This will help to avoid awkward conversations, even with less ill patients, because you can honestly tell them that you ask these questions of all your patients. These issues are particularly imminent with critically ill patients; however, the unexpected can happen with any patient.

Volunteer. Be self-propelled, self-motivated. Volunteer to help with a procedure or a difficult task. Volunteer to give a 20-minute talk on a topic of your choice. Volunteer to take additional patients. Volunteer to stay late. Bring in relevant articles regarding patients and their issues—this shows your enthusiasm, your curiosity, your outside reading, and your interest in evidence-based medicine.

Be a team player. Help other medical students with their tasks; teach them information you have learned. Support your supervising intern or resident whenever possible. Never steal the spotlight, steal a procedure, or make a fellow medical student or resident look bad. Before leaving for the day ask your team if there is anything else you can do to help.

Be prepared. Always have medical tools (stethoscope, reflex hammer, penlight, measuring tape), medical tape, pocket references (often electronic these days), patient information, a small toy for distraction/gaze tracking, and stickers for rewards readily available. That way you will have what you need when you need it, and possibly more importantly, you will have what someone else needs when they are looking for it! The key is to have the necessary items with you without looking like you can barely haul around your heavy white coat.

Be honest. If you don't understand, don't know, or didn't do it, make sure you always say that. Never say or document information that is false (a common example: "bowel sounds normal" when you did not listen).

Present patient information in an organized manner. The presentation of a new patient will be much more thorough than the update given at rounds every morning. Vital information that should be included in a presentation differs by age group. Always begin with a succinct chief complaint, including identifiers (age, sex) and always a symptom, not a diagnosis (e.g., "wheezing," not "asthma")—and its duration. The next line should include important diagnoses carried (e.g., this is where you could state "known asthmatic" or other important information in a wheezer).

Here is a template for the "bullet" presentation for inpatients the days subsequent to admission:

> This is day of hospitalization number for this [age] year old [gender] with a history of [major/pertinent history such as asthma, prematurity, etc. or otherwise healthy] who presented with [major symptoms, such as cough, fever, and chills], and was found to have [working diagnosis]. [Tests done] showed [results]. Yesterday/overnight the patient [state important changes, new plan, new tests, new medications]. This morning the patient feels [state the patient's words], and the physical exam is significant for [state major findings]. Plan is [state plan].

Some patients have extensive histories. The whole history should be present in the admission note, but in a ward presentation it is often too much to absorb. In these cases it will be very much appreciated by your team if you can generate a good summary that maintains an accurate picture of the patient. This usually takes some thought, but it is worth it.

How to Present a Chest Radiograph (CXR)

Always take time to look at each of your patients' radiographs; don't just rely on the report. It is good clinical practice and your attending will likely ask you if you did. Plus, it will help you look like a star on rounds if you have seen the film before.

- First, confirm that the CXR belongs to your patient and is the most recent one.
- If possible, compare to a previous film.

Then, present in a systematic manner:

1. *Technique*
   Rotation, anteroposterior (AP) or posteroanterior (PA), penetration, inspiratory effort (number of ribs visible in lungfields).
2. *Bony structures*
   Look for rib, clavicle, scapula, and sternum fractures.
3. *Airway*
   Look at the glottal area (steeple sign, thumbprint, foreign body, etc), as well as for tracheal deviation, pneumothorax, pneumomediastinum.
4. *Pleural space*
   Look for fluid collections, which can represent hemothorax, chylothorax, pleural effusion.
5. *Lung parenchyma*
   Look for infiltrates and consolidations. These can represent pneumonia, pulmonary contusions, hematoma, or aspiration. The location of an infiltrate can provide a clue to the location of a pneumonia:
   - Obscured right (R) costophrenic angle = right lower lobe
   - Obscured left (L) costophrenic angle = left lower lobe
   - Obscured R heart border = right middle lobe
   - Obscured L heart border = left upper lobe
6. *Mediastinum*
   - Look at size of mediastinum—a widened one (>8 cm) suggests aortic rupture.
   - Look for enlarged cardiac silhouette (>½ thoracic width at base of heart), which may represent congestive heart failure (CHF), cardiomyopathy, hemopericardium, or pneumopericardium.
7. *Diaphragm*
   - Look for free air under the diaphragm (suggests perforation).
   - Look for stomach, bowel, or NG tube above diaphragm (suggests diaphragmatic rupture).
8. *Tubes and lines*
   - Identify all tubes and lines.
   - An endotracheal tube should be 2 cm above the carina. A common mistake is right mainstem bronchus intubation.
   - A chest tube (including the most proximal hole) should be in the pleural space (not in the lung parenchyma).
   - An NGT should be in the stomach and uncoiled.
   - The tip of a central venous catheter (central line) should be in the superior vena cava (not in the right atrium).
   - The tip of a Swan-Ganz catheter should be in the pulmonary artery.
   - The tip of a transvenous pacemaker should be in the right atrium.

A sample CXR presentation may sound like:

This is the CXR of [child's name]. The film is an AP view with good inspiratory effort. There is an isolated fracture of the 8th rib on the right. There is no tracheal deviation or mediastinal shift. There is no pneumo- or hemothorax. The cardiac silhouette appears to be of normal size. The diaphragm and heart borders on both sides are clear, no infiltrates are noted. There is a central venous catheter present, the tip of which is in the superior vena cava. This shows improvement over the CXR from [number of days ago] as the right lower lobe infiltrate is no longer present.

How to Present an Electrocardiogram (ECG)

See chapter on cardiovascular disease for specific rhythms.

- First, confirm that the ECG belongs to your patient and is most recent one.
- If possible, compare to a previous tracing.

Then, present in a systematic manner:

1. Rate (see Figure 1-1)
   "The rate is [number of] beats per minute."
   - The ECG paper is scored so that one big box is .20 seconds. These big boxes consist of five little boxes, each of which are .04 seconds.
   - A quick way to calculate rate when the rhythm is regular is the mantra: 300, 150, 100, 75, 60, 50 (= 300/# large boxes), which is measured as the number of large boxes between two QRS complexes. Therefore, a distance of one large box between two adjacent QRS complexes would be a rate of 300, while a distance of five large boxes between two adjacent QRS complexes would be a rate of 60.
   - For irregular rhythms, count the number of complexes that occur in a 6-second interval (30 large boxes) and multiply by 10 to get a rate in bpm.
2. Rhythm
   "The rhythm is [sinus]/[atrial fibrillation]/[atrial flutter]."
   - If p waves are present in all leads, and upright in leads I & AVF, then the rhythm is sinus. Lack of p waves usually suggests an atrial rhythm. A ventricular rhythm (V Fib or V Tach) is an unstable one (could spell imminent death)—and you should be getting ready for advanced cardiac life support (ACLS).
3. Axis (see Figure 1-2)
   "The axis is [normal]/[deviated to the right]/[deviated to the left]."
   - If I and aVF are both upright or positive, then the axis is normal.
   - If I is upright and aVF is upside down, then there is left axis deviation (LAD).
   - If I is upside down and aVF is upright, then there is right axis deviation (RAD).
   - If I and aVF are both upside down or negative, then there is extreme RAD.
4. Intervals (see Figure 1-3)
   "The [PR]/[QRS] intervals are [normal]/[shortened]/[widened]."
   - Normal PR interval = .12–.20 seconds.
   - Short PR is associated with Wolff-Parkinson-White syndrome (WPW).
   - Long PR interval is associated with heart block of which there are three types:
     - First-degree block: PR interval >.20 seconds (one big box).
     - Second-degree (Wenckebach) block: PR interval lengthens progressively until a QRS is dropped.
     - Second-degree (Mobitz) block: PR interval is constant, but one QRS is dropped at a fixed interval.
     - Third-degree block: Complete AV dissociation, prolonged presence is incompatible with life.
   - Normal QRS interval ≤.12 seconds.
   - Prolonged QRS is seen when the beat is initiated in the ventricle rather than the sinoatrial node, when there is a bundle branch block, and when the heart is artificially paced with longer QRS intervals. Prolonged QRS is also noted in tricyclic overdose and WPW.
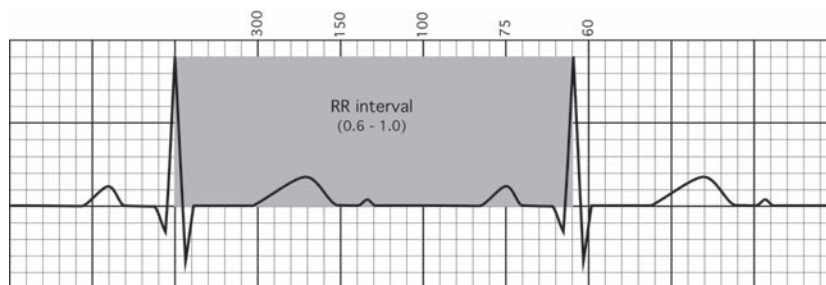
FIGURE 1-1.   ECG rate.
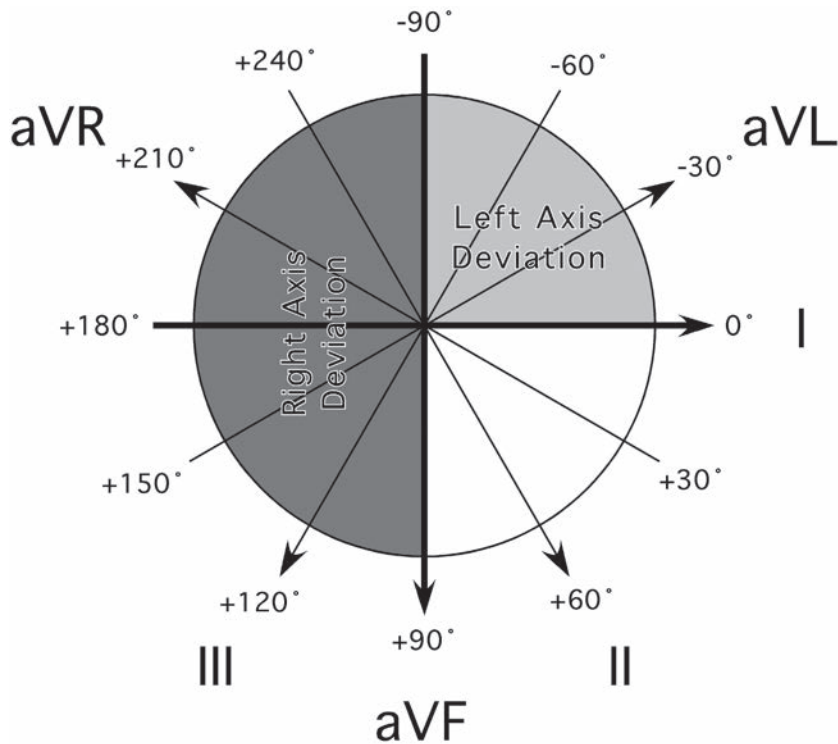
FIGURE 1-2. **ECG axes.**
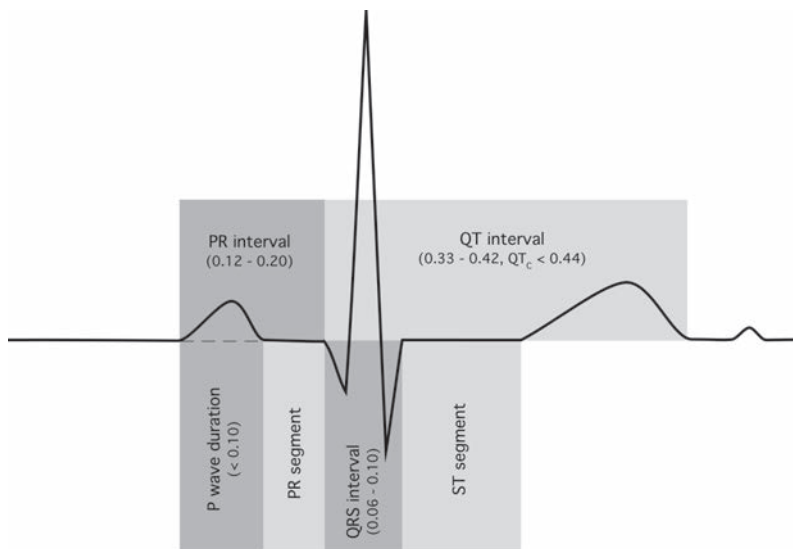
FIGURE 1-3. **ECG segments.**

5. Wave morphology (see Figure 1-4)
   a. Ventricular hypertrophy
      ■ "There [is/is no] [left/right] [ventricular/atrial] hypertrophy."
   b. Atrial hypertrophy
      ■ Clue is presence of tall p waves.
   c. Ischemic changes
      ■ "There [are/are no] S-T wave [depressions/elevations] or [flattened/
        inverted] T waves." Presence of Q wave indicates an old infarct.

(*continued*)
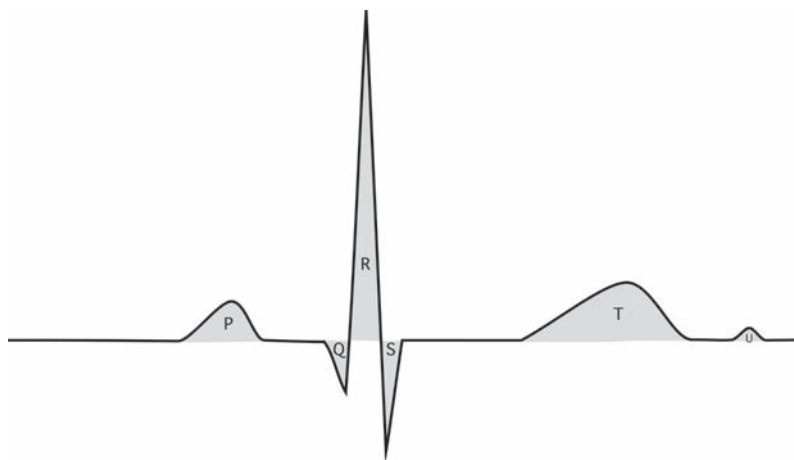
FIGURE 1-4. ECG waves.

> **d.** Bundle branch block (BBB)
> - "There [is/is no] [left/right] bundle branch block."
> - Clues:
>   - Presence of RSR' wave in leads V1–V3 with ST depression and T wave inversion goes with RBBB.
>   - Presence of notched R wave in leads I, aVL, and V4–V6 goes with LBBB.

On Outpatient

The ambulatory part of the pediatrics rotation consists of mainly two parts—focused histories and physicals for acute problems and well-child visits. In the general pediatrics clinic, you will see the common ailments of children, but don't overlook the possibility of less common ones. Usually, you will see the patient first, to take the history and do the physical exam. It is important to strike a balance between obtaining a thorough exam and not upsetting the child so much that the attending won't be able to recheck any pertinent parts of it. For acute cases, present the patient distinctly, including an appropriate differential diagnosis and plan. In this section, be sure to include possible etiologies, such as specific bacteria, as well as a specific treatment (e.g., a particular antibiotic, dose, and course of treatment). For presentation of well-child visits, cover all the bases, but focus on the patients' concerns and your findings. There are specific issues to discuss depending on the age of the child. Past history and development is important, but so is anticipatory guidance–prevention and expectations for what is to come. The goal is to be both efficient and thorough.

> **Pediatric History and Physical Exam**
>
> **HISTORY**
>
> **ID/CC:** Age, sex, symptom, duration
> **HPI:** This should be presented in an organized and concise way, leading up to the day of admission or the day of presentation. Avoid using actual dates and days of the week. Avoid superfluous details which will not influence your differential diagnosis.
> **A good opening line for your HPI:** This is a 4-year-old male with no significant past medical history, who was in his usual state of good health until 3 days prior to admission when . . .
>
> *(continued)*

In the HPI, include:

Symptoms—location, quality, quantity, aggravating and alleviating factors (make sure to include all pertinent positive and pertinent negative symptoms)
Time course—onset, duration, frequency, change over time
Rx/Intervention—medications, medical help sought, other actions taken Exposures, ill contacts, travel

Current Health:

Nutrition—breast milk/formula/food, quantity, frequency, supplements, problems (poor suck/swallow, reflux)
Sleep—quantity, quality, disturbances (snoring, apnea, bedwetting, restlessness), intervention, wakes up refreshed
Elimination—bowel movement frequency/quality, urination frequency, problems, toilet training
Behavior—toward family, friends, discipline
Development—gross motor, fine motor, language, cognition, social/emotional

PMH:

Pregnancy (be sensitive to adoption issues)—gravida/para status, maternal age, duration, exposures (medications, alcohol, tobacco, drugs, infections, radiation); complications (bleeding, gestational diabetes, hypertension, etc), occurred on contraception?, planned?, emotions regarding pregnancy, problems with past pregnancies
Labor and delivery—length of labor, rupture of membranes, fetal movement, medications, presentation/delivery, mode of delivery, assistance (forceps, vacuum), complications, Apgars, immediate breathe/cry, oxygen requirement/intubation, and duration
Neonatal—birth height/weight, abnormalities/injuries, length of hospital stay, complications (respiratory distress, cyanosis, anemia, jaundice, seizures, anomalies, infections), behavior, maternal concerns
Infancy—temperament, feeding, family reactions to infant
Illnesses/hospitalizations/surgeries/accidents/injuries—dates, medications/ interventions, impact on child/family—don't forget circumcision
Medications—past (antibiotics, especially), present, reactions
Allergies—include reaction
Immunizations—up to date, reactions
Family history—relatives, ages, health problems, deaths (age/cause), miscarriages/ stillbirths/deaths of infants or children, health status of parents and siblings, pertinent negative family history
Social history—parents' education and occupation, living arrangements, pets, water (city or well), lead exposure (old house, paint), smoke exposure, religion, finances, family dynamics, risk-taking behaviors, school/daycare, other caregivers, HEADDSSS exam for adolescents (see Health Supervision and Prevention of Illness and Injury in Children and Adolescents chapter)

ROS:

General—fever, activity, growth
Head—trauma, size, shape
Eyes—erythema, drainage, acuity, tearing, trauma
Ears—infection, drainage, hearing
Nose—drainage, congestion, sneezing, bleeding, frequent colds
Mouth—eruption/condition of teeth, lesions, infection, odor
Throat—sore, tonsils, recurrent strep pharyngitis
Neck—stiff, lumps, tenderness
Respiratory—cough, wheeze, chest pain, pneumonia, retractions, apnea, stridor
Cardiovascular—murmur, exercise intolerance, diaphoresis, syncope
Gastrointestinal—appetite, constipation, diarrhea, poor suck, swallow, abdominal pain, jaundice, vomiting, change in bowel movements, blood, food intolerances

(continued)

GU—urine output, stream, urgency, frequency, discharge, blood, fussy during menstruation, sexually active
Endocrine—polyuria/polydipsia/polyphagia, puberty, thyroid, growth/stature
Musculoskeletal—pain, swelling, redness, warmth, movement, trauma
Neurologic—headache, dizziness, convulsions, visual changes, loss of consciousness, gait, coordination, handedness
Skin—bruises, rash, itching, hair loss, color (cyanosis)
Lymph—swelling, redness, tender glands

PHYSICAL EXAM

General—smiling, playful, cooperative, irritable, lethargic, tired, hydration status
Vitals—temperature, heart rate, respiratory rate, blood pressure, pulse ox
Growth—weight, height, head circumference (include percentiles), BMI if applicable
Skin—inspect, palpate, birthmarks, rash, jaundice, cyanosis
Head—normocephalic, atraumatic, anterior fontanelle, sutures
Eyes—redness, swelling, discharge, red reflex, strabismus, scleral icterus
Ears—tympanic membranes (DO LAST!)
Nose—patent nares, flaring nostrils
Mouth—teeth, palate, thrush
Throat—oropharynx (red, moist, injection, exudate)
Neck—range of motion, meningeal signs
Lymph—cervical, axillary, inguinal
Cardiovascular—heart rate, murmur, rub, pulses (central/peripheral; bilateral upper and lower extremities including femoral), perfusion/color
Respiratory—rate, retractions, grunting, crackles, wheezes
Abdomen—bowel sounds, distention, tenderness, hepatosplenomegaly, masses, umbilicus, rectal
Back—scoliosis, dimples
Musculoskeletal—joints—erythema, warmth, swelling tenderness, range of motion
Neurologic—gait, symmetric extremity movement, strength/tone/bulk, reflexes (age-appropriate and deep tendon reflexes), mentation, coordination
Genitalia—circumcision, testes, labia, hymen, Tanner staging

Note: The COMSEP website (http://comsep.org) has a video clip demonstrating the pediatric physical exam. It can be found under "curriculum" then "curriculum support resources."

Your Rotation Grade

Usually, the clerkship grade is broken down into three or four components (every medical school divides grade differently, check with your school's grading policy):

- *Inpatient evaluation:* This includes evaluation of your ward time by residents and attendings and is based on your performance on the ward.
- *Ambulatory evaluation:* This includes your performance in clinic, including clinic notes and any procedures performed in the outpatient setting.
- *National Board of Medical Examiners (NBME) examination:* This portion of the grade is anywhere from 20% to 50%, so performance on this multiple-choice test is vital to achieving honors in the clerkship.
- *Objective Structured Clinical Examination (OSCE) or oral exam:* Some schools now include an OSCE or oral exam as part of their clerkship evaluation. This is basically an exam that involves standardized patients and allows assessment of a student's bedside manner and physical examination skills.

How to Study

Make a list of core material to learn. This list should reflect common symptoms, illnesses, and areas in which you have particular interest or in which you feel particularly weak. Do not try to learn every possible topic.

SYMPTOMS

- Fever
- Failure to thrive
- Sore throat
- Wheezing/cough
- Vomiting
- Diarrhea
- Abdominal pain
- Jaundice
- Fluid and electrolyte imbalance
- Seizures

The knowledge you need on the wards is the day-to-day management know-how (though just about anything is game for pimping!). The knowledge you want by the end-of-rotation examination is the epidemiology, risk factors, pathophysiology, diagnosis, and treatment of major diseases seen in pediatrics.

As you see patients, note their major symptoms and diagnosis for review. Your reading on the symptom-based topics above should be done with a specific patient in mind. For example, if a patient comes in with diarrhea, read about common infectious causes of gastroenteritis and the differences between and complications of them, noninfectious causes, and dehydration in the review book that night.

Select your study material. We recommend the following:

- The review book, *First Aid for the Pediatrics Clerkship*
- A major pediatric textbook—*Nelson's Textbook of Pediatrics* (also available on MD Consult) and its very good counterpart, *Nelson's Essentials*
- *The Harriet Lane Handbook*—the bible of pediatrics: medicine, medications, and lab values as they apply to children

Prepare a talk on a topic. You may be asked to give a small talk once or twice during your rotation. If not, you should volunteer! Feel free to choose a topic that is on your list; however, realize that the people who hear the lecture may consider this dull. The ideal topic is slightly uncommon but not rare, for example, Kawasaki disease. To prepare a talk on a topic, read about it in a major textbook and a review article not more than 2 years old. Then search online or in the library for recent developments or changes in treatment.

Procedures. You may have the opportunity to perform a couple of procedures on your pediatrics rotation. Be sure to volunteer to do them whenever you can, and at least actively observe if participation is not allowed. These may include:

- Lumbar puncture
- Intravenous line placement
- NGT placement
- Venipuncture (blood draw)
- Foley (urinary) catheter placement

- Transillumination of scrotum
- IM/SQ immunization injections
- Rapid strep or throat culture
- Nasopharyngeal swabs or cultures

How to Prepare for the Clinical Clerkship Examination

If you have read about your core illnesses and core symptoms, you will know a great deal about pediatrics. It is difficult but vital to balance reading about your specific patients and covering all of the core topics of pediatrics. To study for the clerkship exam, we recommend:

2–3 weeks before exam: Read this entire review book, taking notes.
10 days before exam: Read the notes you took during the rotation on your core content list, and the corresponding review book sections.
5 days before exam: Read the entire review book, concentrating on lists and mnemonics.
2 days before exam: Exercise, eat well, skim the book, and go to bed early.
1 day before exam: Exercise, eat well, review your notes and the mnemonics, and go to bed on time. Do not have any caffeine after 2 PM

Throughout all your studying do practice questions from a reliable source of questions.

Other helpful studying strategies include:

Study with friends. Group studying can be very helpful. Other people may point out areas that you have not studied enough and may help you focus on the goal. If you tend to get distracted by other people in the room, limit this to less than half of your study time.

Study in a bright room. Find the room in your house or in your library that has the best, brightest light. This will help prevent you from falling asleep. If you don't have a bright light, get a halogen desk lamp or a light that simulates sunlight (not a tanning lamp).

Eat light, balanced meals. Make sure your meals are balanced, with lean protein, fruits and vegetables, and fiber. A high-sugar, high-carbohydrate meal will give you an initial burst of energy for 1 to 2 hours, but then you'll drop.

Take practice exams. The point of practice exams is not so much the content that is contained in the questions, but the training of sitting still for 3 hours and trying to pick the best answer for each and every question.

Tips for answering questions. All questions are intended to have one best answer. When answering questions, follow these guidelines:

Read the answers first. For all questions longer than two sentences, reading the answers first can help you sift through the question for the key information. **Look for the words "EXCEPT, MOST, LEAST, NOT, BEST, WORST, TRUE, FALSE, CORRECT, INCORRECT, ALWAYS, and NEVER."** If you find one of these words, circle or underline it for later comparison with the answer.

Finally, remember—children are not just small adults. They present with a whole new set of medical and social issues. More than ever, you are treating families, not just individual patients.

Pocket Cards for the Wards

The following "cards" contain information that is often helpful during the pediatrics rotation. We advise that you make a copy of these cards, cut them out, and carry them in your coat pocket when you are on the wards.

Recommended Immunization Schedule for Persons Aged 0–6 Years—UNITED STATES • 2007

Vaccine ▼	Birth	1 month	2 months	4 months	6 months	12 months	15 months	18 months	19–23 months	2–3 years	4–6 years
Hepatitis B[1]	HepB	HepB		see footnote 1	HepB			HepB Series			
Rotavirus[2]			Rota	Rota	Rota						
Diphtheria, Tetanus, Pertussis[3]			DTaP	DTaP	DTaP		DTaP				DTaP
Haemophilus influenzae type b[4]			Hib	Hib	Hib[4]	Hib					
Pneumococcal[5]			PCV	PCV	PCV	PCV		PCV		PPV	
Inactivated Poliovirus			IPV	IPV		IPV					IPV
Influenza[6]						Influenza (Yearly)					
Measles, Mumps, Rubella[7]						MMR					MMR
Varicella[8]						Varicella					Varicella
Hepatitis A[9]						HepA (2 doses)			HepA Series		
Meningococcal[10]										MPSV4	

Range of recommended ages
Catch-up immunization
Certain high-risk groups

This schedule indicates the recommended ages for routine administration of currently licensed childhood vaccines, as of December 1, 2006, for children aged 0–6 years. Additional information is available at **http://www.cdc.gov/nip/recs/child-schedule.htm**. Any dose not administered at the recommended age should be administered at any subsequent visit, when indicated and feasible. Additional vaccines may be licensed and recommended during the year. Licensed combination vaccines may be used whenever any components of the combination are indicated and other components of the vaccine are not contraindicated and if approved by the Food and Drug Administration for that dose of the series. Providers should consult the respective Advisory Committee on Immunization Practices statement for detailed recommendations. Clinically significant adverse events that follow immunization should be reported to the Vaccine Adverse Event Reporting System (VAERS). Guidance about how to obtain and complete a VAERS form is available at http://www.vaers.hhs.gov or by telephone, 800-822-7967. **FOOTNOTES ON REVERSE SIDE**

FOOTNOTES
1. Hepatitis B vaccine (HepB). *(Minimum age: birth)*
  At birth:
  • Administer monovalent HepB to all newborns before hospital discharge.
  • If mother is hepatitis surface antigen (HBsAg)-positive, administer HepB and 0.5 mL of hepatitis B immune globulin (HBIG) within 12 hours of birth.
  • If mother's HBsAg status is unknown, administer HepB within 12 hours of birth. Determine the HBsAg status as soon as possible and if HBsAg-positive, administer HBIG (no later than age 1 week).
  • If mother is HBsAg-negative, the birth dose can only be delayed with physician's order and mother's negative HBsAg laboratory report documented in the infant's medical record.
  After the birth dose:
  • The HepB series should be completed with either monovalent HepB or a combination vaccine containing HepB. The second dose should be administered at age 1–2 months. The final dose should be administered at age ≥ 24 weeks. Infants born to HBsAg-positive mothers should be tested for HBsAg and antibody to HBsAg after completion of ≥ 3 doses of a licensed HepB series, at age 9–18 months (generally at the next well-child visit).
  4-month dose:
  • It is permissible to administer 4 doses of HepB when combination vaccines are administered after the birth dose. If monovalent HepB is used for doses after the birth dose, a dose at age 4 months is not needed.
2. Rotavirus vaccine (Rota). *(Minimum age: 6 weeks)*
  • Administer the first dose at age 6–12 weeks. Do not start the series later than age 12 weeks.
  • Administer the final dose in the series by age 32 weeks. Do not administer a dose later than age 32 weeks.
  • Data on safety and efficacy outside of these age ranges are insufficient.
3. Diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP). *(Minimum age: 6 weeks)*
  • The fourth dose of DTaP may be administered as early as age 12 months, provided 6 months have elapsed since the third dose.
  • Administer the final dose in the series at age 4–6 years.
4. Haemophilus influenzae type b conjugate vaccine (Hib). *(Minimum age: 6 weeks)*
  • If PRP-OMP (PedvaxHIB® or ComVax® [Merck]) is administered at ages 2 and 4 months, a dose at age 6 months is not required.
  • TriHiBit® (DTaP/Hib) combination products should not be used for primary immunization but can be used as boosters following any Hib vaccine in children aged ≥ 12 months.
5. Pneumococcal vaccine. *(Minimum age: 6 weeks for pneumococcal conjugate vaccine [PCV]; 2 years for pneumococcal polysaccharide vaccine [PPV])*
  • Administer PCV at ages 24–59 months in certain high-risk groups. Administer PPV to children aged ≥ 2 years in certain high-risk groups. See MMWR 2000;49(No. RR-9);1–35.
6. Influenza vaccine. *(Minimum age: 6 months for trivalent inactivated influenza vaccine [TIV]; 5 years for live, attenuated influenza vaccine [LAIV])*
  • All children aged 6–59 months and close contacts of all children aged 0–59 months are recommended to receive influenza vaccine.
  • Influenza vaccine is recommended annually for children aged ≥ 59 months with certain risk factors, health-care workers, and other persons (including household members) in close contact with persons in groups at high risk. See MMWR 2006;55(No. RR-10);1–41.
  • For healthy persons aged 5–49 years, LAIV may be used as an alternative to TIV.
  • Children receiving TIV should receive 0.25 mL if aged 6–35 months or 0.5 mL if aged ≥ 3 years.
  • Children aged <9 years who are receiving influenza vaccine for the first time should receive 2 doses (separated by ≥ 4 weeks for TIV and ≥ 6 weeks for LAIV).
7. Measles, mumps, and rubella vaccine (MMR). *(Minimum age: 12 months)*
  • Administer the second dose of MMR at age 4–6 years. MMR may be administered before age 4–6 years, provided ≥ 4 weeks have elapsed since the first dose and both doses are administered at age ≥ 12 months.
8. Varicella vaccine. *(Minimum age: 12 months)*
  • Administer the second dose of varicella vaccine at age 4–6 years. Varicella vaccine may be administered before age 4–6 years, provided that ≥ 3 months have elapsed since the first dose and both doses are administered at age ≥ 28 days following the first dose. The second dose does not need to be repeated.
9. Hepatitis A vaccine (HepA). *(Minimum age: 12 months)*
  • HepA is recommended for all children aged 1 year (i.e., aged 12–23 months). The 2 doses in the series should be administered at least 6 months apart.
  • Children not fully vaccinated by age 2 years can be vaccinated at subsequent visits.
  • HepA is recommended for certain other groups of children, including in areas where vaccination programs target older children. See MMWR 2006;55(No. RR-7);1–23.
10. Meningococcal polysaccharide vaccine (MPSV4). *(Minimum age: 2 years)*
  • Administer MPSV4 to children aged 2–10 years with terminal complement deficiencies or anatomic or functional asplenia and certain other high-risk groups. See MMWR 2005;54(No. RR-7);1–21.

CS108190

Recommended Immunization Schedule for Persons Aged 7–18 Years—UNITED STATES • 2007

Vaccine ▼ Age ▶	7–10 years	11–12 YEARS	13–14 years	15 years	16–18 years
Tetanus, Diphtheria, Pertussis[1]	see footnote 1	Tdap	Tdap		
Human Papillomavirus[2]	see footnote 2	HPV (3 doses)	HPV Series		
Meningococcal[3]	MPSV4	MCV4	MCV4[3] MCV4		
Pneumococcal[4]		PPV			
Influenza[5]		Influenza (Yearly)			
Hepatitis A[6]		HepA Series			
Hepatitis B[7]		HepB Series			
Inactivated Poliovirus[8]		IPV Series			
Measles, Mumps, Rubella[9]		MMR Series			
Varicella[10]		Varicella Series			

Range of recommended ages

Catch-up immunization

Certain high-risk groups

This schedule indicates the recommended ages for routine administration of currently licensed childhood vaccines, as of December 1, 2006, for children aged 7–18 years. Additional information is available at **http://www.cdc.gov/nip/recs/child-schedule.htm.** Any dose not administered at the recommended age should be administered at any subsequent visit, when indicated and feasible. Additional vaccines may be licensed and recommended during the year. Licensed combination vaccines may be used whenever any components of the combination are indicated and other components of the vaccine are not contraindicated and if approved by the Food and Drug Administration for that dose of the series. Providers should consult the respective Advisory Committee on Immunization Practices statement for detailed recommendations. Clinically significant adverse events that follow immunization should be reported to the Vaccine Adverse Event Reporting System (VAERS). Guidance about how to obtain and complete a VAERS form is available at **http://www.vaers.hhs.gov** or by telephone, **800-822-7967. FOOTNOTES ON REVERSE SIDE**

FOOTNOTES
1. **Tetanus and diphtheria toxoids and acellular pertussis vaccine (Tdap).** *(Minimum age: 10 years for BOOSTRIX® and 11years for ADACEL™)*
   • Administer at age 11–12 years for those who have completed the recommended childhood DTP/DTaP vaccination series and have not received a tetanus and diphtheria toxoids vaccine (Td) booster dose.
   • Adolescents aged 13–18 years who missed the 11–12 year Td/Tdap booster dose should also receive a single dose of Tdap if they have completed the recommended childhood DTP/DTaP vaccination series.
2. **Human papillomavirus vaccine (HPV).** *(Minimum age: 9 years)*
   • Administer the first dose of the HPV vaccine series to females at age 11–12 years.
   • Administer the second dose 2 months after the first dose and the third dose 6 months after the first dose.
   • Administer the HPV vaccine series to females at age 13–18 years if not previously vaccinated.
3. **Meningococcal vaccine.** *(Minimum age: 11 years for meningococcal conjugate vaccine [MCV4]; 2 years for meningococcal polysaccharide vaccine [MPSV4])*
   • Administer MCV4 at age 11–12 years and to previously unvaccinated adolescents at high school entry (at approximately age 15 years).
   • Administer MCV4 to previously unvaccinated college freshmen living in dormitories; MPSV4 is an acceptable alternative.
   • Vaccination against invasive meningococcal disease is recommended for children and adolescents aged ≥ 2 years with terminal complement deficiencies or anatomic or functional asplenia and certain other high-risk groups. See *MMWR* 2005;54(No. RR-7):1–21. Use MPSV4 for children aged 2–10 years and MCV4 or MPSV4 for older children.
4. **Pneumococcal polysaccharide vaccine (PPV).** *(Minimum age: 2 years)*
   • Administer for certain high-risk groups. See *MMWR* 1997;46(No. RR-8):1–24, and *MMWR* 2000;49(No. RR-9):1–35.
5. **Influenza vaccine.** *(Minimum age: 6 months for trivalent inactivated influenza vaccine [TIV]; 5 years for live, attenuated influenza vaccine [LAIV])*
   • Influenza vaccine is recommended annually for persons with certain risk factors, health-care workers, and other persons (including house-hold members) in close contact with persons in groups at high risk. See *MMWR* 2006;55(No. RR-10):1–41.
   • For healthy persons aged 5–49 years, LAIV may be used as an alternative to TIV.
   • Children aged < 9 years who are receiving influenza vaccine for the first time should receive 2 doses (separated by ≥ 4 weeks for TIV and ≥ 6 weeks for LAIV).
6. **Hepatitis A vaccine (HepA).** *(Minimum age: 12 months)*
   • The 2 doses in the series should be administered at least 6 months apart.
   • HepA is recommended for certain other groups of children, including in areas where vaccination programs target older children. See *MMWR* 2006;55(No. RR-7):1–23.
7. **Hepatitis B vaccine (HepB).** *(Minimum age: birth)*
   • Administer the 3-dose series to those who were not previously vaccinated.
   • A 2-dose series of Recombivax HB® is licensed for children aged 11–15 years.
8. **Inactivated poliovirus vaccine (IPV).** *(Minimum age: 6 weeks)*
   • For children who received an all-IPV or all-oral poliovirus (OPV) series, a fourth dose is not necessary if the third dose was administered at age ≥ 4 years.
   • If both OPV and IPV were administered as part of a series, a total of 4 doses should be administered, regardless of the child's current age.
9. **Measles, mumps, and rubella vaccine (MMR).** *(Minimum age: 12 months)*
   • If not previously vaccinated, administer 2 doses of MMR during any visit, with ≥ 4 weeks between the doses.
10. **Varicella vaccine.** *(Minimum age: 12 months)*
   • Administer 2 doses of varicella vaccine to persons without evidence of immunity.
   • Administer 2 doses of varicella vaccine to persons aged < 13 years at least 3 months apart. Do not repeat the second dose, if administered ≥ 28 days after the first dose.
   • Administer 2 doses of varicella vaccine to persons aged ≥ 13 years at least 4 weeks apart.

CS108190

High-Yield Facts

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Gestation and Birth

Embryology

GESTATIONAL/EMBRYOLOGIC LANDMARKS

See Table 2-1.

GERM LAYERS

See Table 2-2.

HEART

- **Week 3**: Paired heart tubes begin to work.
- **Week 4:**
  - Primordial atrium is divided into left and right by septa primum and secundum.
  - Septum primum forms the valve of the foramen ovale, which closes about 3 months after birth.
  - Failure of the foramen ovale to close results in an **atrial septal defect (ASD)**.
- **Week 7:**
  - The single ventricle is divided into left and right; prior to that the interventricular foramen communicates between left and right sides.
  - Failure of the interventricular foramen to close results in a **ventricular septal defect (VSD)**.

TABLE 2-1. Gestational/Embryologic Landmarks

Week 1	Fertilization, usually in fallopian tube ampulla
	Implantation begins
Week 2	Implantation complete
	Endoderm and ectoderm form (bilaminar embryo)
Week 3	Mesoderm formed (trilaminar embryo)
Week 5	Subdivisions of forebrain, midbrain, and hindbrain are formed
Week 7	Heart formed
Week 8	Primary organogenesis complete
	Placentation occurs
Week 9	Permanent kidneys begin functioning
Week 10	Midgut returns from umbilical cord, where it was developing, to abdominal cavity, while undergoing counterclockwise rotation
Week 24	Primitive alveoli are formed and surfactant production begins
Week 26	Testicles descend

T A B L E 2 - 2 . **Summary of Germ Layer Derivatives**

Ectoderm	Neural Crest Cells (Ectoderm)	Mesoderm	Endoderm
CNS, peripheral nervous system (PNS)	Spinal nerves; cranial nerves V, VII, IX, X; sensory neurons	Connective tissue, cartilage, bone	Epithelial lining of gastrointestinal tract, respiratory tract, and middle ear, including eustachian tube
Sensory epithelia of eye, ear, nose	Autonomic ganglia	Striated and smooth muscle	
Epidermis, hair, nails	Adrenal medulla	Blood and lymphatic systems	Tonsil parenchyma
Mammary glands, pituitary gland, subcutaneous glands	Meninges	Ovaries, testes, genital ducts	Thymus
Tooth enamel	Pigment cells, glial cells of peripheral nerves	Serous membranes lining body cavities	Parathyroid and thyroid glands
		Spleen, adrenal cortex	Liver, pancreas

CIRCULATION

- See Figure 2-1.
  Umbilical vein = oxygenated blood
  Umbilical artery = deoxygenated blood
- Well-oxygenated blood returns from placenta through umbilical vein, where half of it enters the inferior vena cava through the ductus venosus (continuation of the umbilical vein beyond the branching of the left and right portal veins), and the rest enters the hepatic circulation (preferentially through the left portal vein).
- Despite the fact that the umbilical venous blood joins the inferior vena cava prior to entering the right atrium, the streams do not mix substantially. Blood from the artery to vein is preferentially shunted through the foramen ovale to the left atrium, while blood from the lower inferior vena cava, right hepatic circulation, and superior vena cava enters the right ventricle.

> **WARD TIP**
>
> Closure of the ductus arteriosus can be prevented by prostaglandin E_1 and facilitated by indomethacin (via inhibition of prostaglandin synthesis).
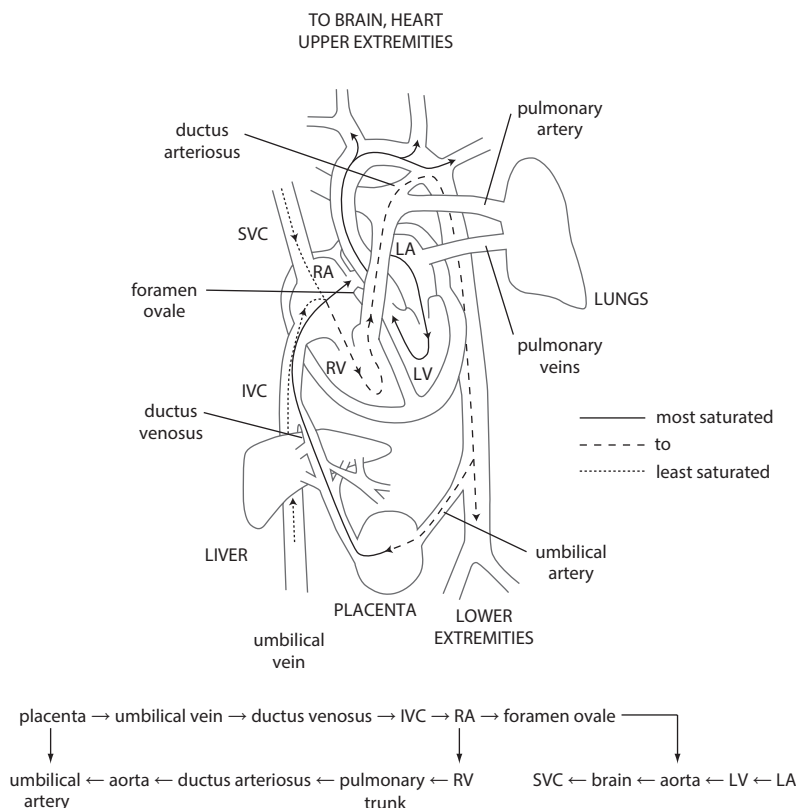

placenta → umbilical vein → ductus venosus → IVC → RA → foramen ovale

umbilical artery ← aorta ← ductus arteriosus ← pulmonary trunk ← RV

SVC ← brain ← aorta ← LV ← LA

F I G U R E 2 - 1 . **Fetal circulation.**

- The major portion of blood exiting the right ventricle is then shunted to the aorta through the ductus arteriosus because the lungs are collapsed and pulmonary artery pressures are high.
- Sixty-five percent of blood in the descending aorta returns to the umbilical arteries for reoxygenation at the placenta; the remainder supplies the inferior part of the body.
- After birth, pulmonary artery pressure drops because the lungs expand, reducing flow across the ductus arteriosus and stimulating its closure (usually within first few days of life). (See Figure 2-2.)
- Pressure in the left atrium becomes higher than that in the right atrium after birth due to the ↑ pulmonary return, which stimulates closure of the foramen ovale (usually complete by third month of life).

HEMOGLOBIN

Fetal erythropoiesis occurs in the yolk sac (3–8 weeks), liver (6–8 weeks), spleen (9–28 weeks), and then bone marrow (28 weeks onward).

GENITOURINARY TRACT

- Metanephri (permanent kidneys) start functioning at 9 weeks; urine is excreted into amniotic cavity.
- Initially, kidneys lie in the pelvis; by 8 weeks they migrate into their adult position.
- Morphologic sexual characteristics do not develop until 7 weeks' gestation.
- In males, testis-determining factor induces primary sex cords to develop as male gonads, with testosterone production by 8 weeks.
- Testicles develop intra-abdominally and then descend through inguinal canals into the scrotum by 26 weeks.
- Ovaries are identified by 10 weeks; primary sex cords develop into female gonads with primordial follicles developing prenatally.

GASTROINTESTINAL TRACT

- By 10 weeks, the midgut returns from the umbilical cord, where it was developing, to the abdominal cavity while undergoing counterclockwise rotation.
- Insufficient rotation of the midgut, called **malrotation,** can present in neonatal period as intestinal obstruction.
- Incomplete separation of foregut and primitive airway can → **trachea-esophageal fistula (TEF).**
- Failure of the intestine to return to the abdominal cavity with intestinal contents remaining at the base of the umbilical cord causes **gastroschisis,** a full-thickness abdominal wall defect with extruded intestine.
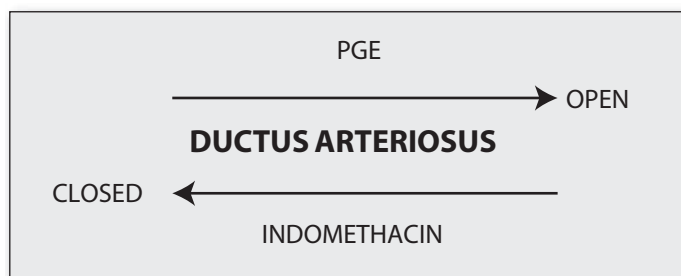
PGE

→ OPEN

DUCTUS ARTERIOSUS

CLOSED ←

INDOMETHACIN

FIGURE 2-2.   **Mechanism of ductus arteriosus patency/closure.**

LUNGS

By 24 weeks, primitive alveoli are formed and surfactant production is begun.

CENTRAL NERVOUS SYSTEM (CNS)

- During week 3, the neural tube is formed on the ectodermal surface.
- Neural tube openings (rostral and caudal) are closed by 25–27 days.
- By week 5, subdivisions of forebrain, midbrain, and hindbrain are formed.
- Failure of caudal neural tube to close completely can result in **spina bifida** (unfused vertebral arch with or without unfused dura mater and spinal cord), commonly seen in the lumbar area. Failure of the rostral neural tube to close can result in anencephaly.
- Folate supplementation helps prevent neural tube defects.
- Excessive alcohol use during pregnancy can result in neural tube defect due to deficiency of folate.

Placenta

DEVELOPMENT

- Fetal portion of placenta is formed from chorionic sac.
- Maternal portion is derived from endometrium.

TRANSPORT

- Nutrients, electrolytes, water, and gases are diffused or transported across the placenta.
- Most drugs pass through placenta and can be detected in fetal plasma (e.g., warfarin, morphine, propylthiouracil, and drugs of abuse).
- A few substances cannot pass because of their size or charge (e.g., heparin); protein hormones (e.g., insulin) do not cross placenta.

METABOLISM

Placenta synthesizes glycogen and cholesterol.

ENDOCRINE FUNCTION

Placenta produces β-human chorionic gonadotropin (β-hCG), human chorionic adrenocorticotropic hormone (ACTH), human placental lactogen, and human chorionic somatomammotropin.

Prenatal Disturbances

INFECTIONS

Infants who have experienced an intrauterine infection have a higher-than-average incidence of being small for gestational age, hepatosplenomegaly, congenital defects, microcephaly, and intracranial calcifications.

EXAM TIP

Lecithin-to-sphingomyelin ratio in the amniotic fluid greater than 3 indicates fetal lung maturity.

EXAM TIP

Folic acid supplements during pregnancy reduce incidence of neural tube defects.

EXAM TIP

Maternal α-fetoprotein (AFP) is *high in*:
- Multiple gestations (most common)
- Fetal neural tube defects
- Gastroschisis

WARD TIP

Testing urine for β-hCG allows early detection of pregnancy.

EXAM TIP

Maternal AFP is *low* in trisomies 21 (Down syndrome) and 18.

FIGURE 2-3. Fetal alcohol syndrome. Notice the depressed nasal bridge, flat philtrum, long upper lip, and thin vermillion border. (Reproduced with permission from Stoler JM, Holmes LB. Underrecognition of prenatal alcohol effects in infants of known alcohol abusing women, J Pediatr. 1999 Oct;135(4):430–436.)

Toxoplasmosis

- Maternal infection is due to ingestion of oocysts from feces of infected cats and is asymptomatic.
- Clinical features in infants include microcephaly, hydrocephalus, intracranial calcifications, chorioretinitis, and seizures.

Rubella

- Congenital rubella syndrome is rare due to the effectiveness of the rubella vaccine.
- Maternal infection early in pregnancy can result in congenital rubella syndrome, which includes meningoencephalitis, microcephaly, cataracts, sensorineural hearing loss, and congenital heart disease (patent ductus arteriosus and pulmonary artery stenosis).

Cytomegalovirus (CMV)

- Common—occurs in 1% of newborns.
- Newborn disease is associated with primary maternal infection with a 50% chance of infection.
- In those affected, only 5% have neurologic deficits.
- Infection occurs in 1% of pregnancies with recurrent or reactivated infection.
- CMV transmitted intrapartum, through infected blood or through breast milk, is not associated with neurologic deficits.
- Clinical features include intrauterine growth retardation (IUGR), low birth weight, petechiae and purpura, jaundice and hepatosplenomegaly, microcephaly, chorioretinitis, and intracranial calcifications.
- Late manifestations like learning and hearing deficits can occur in 10% of clinically inapparent infections.

TOXINS AND TERATOGENS

Alcohol

- Most common teratogen.
- The amount of alcohol consumed correlates with the severity of spectrum of effects in the neonate, ranging from mild reduction in cerebral function to classic fetal alcohol syndrome (see Figure 2-3).
- Clinical manifestations include microcephaly and mental retardation, IUGR, facial dysmorphism (midfacial hypoplasia, micrognathia, shortened nasal philtrum, short palpebral fissures, and a thin vermillion border), renal and cardiac defects, and hypospadias.
- Alcohol use during pregnancy also increases risk of neural tube defects.

Cocaine

Term, 5-lb, 2-day-old infant has irritability, nasal stuffiness, and coarse tremors. He feeds poorly and has diarrhea. *Think: Cocaine or heroin withdrawal.*

Cocaine readily crosses the placental barrier, placing the fetus at risk. Symptoms of cocaine withdrawal include tremors, high-pitched cry, irritability, excess suck, apnea, and tachycardia, which can become evident within the first 72 hours of life. Opiates also cross the placenta. Tremor and irritability are the common symptoms of opiate withdrawal. Vague autonomic symptoms such as yawning and sneezing are often present. Obtain urine drug screen and meconium screen if opioid use in the mother is suspected.

- Causes maternal hypertension and constriction of placental circulation → ↓ uterine blood flow and fetal hypoxia.
- Associated with a higher risk of spontaneous abortion, placental abruption, fetal distress, meconium staining, preterm birth, IUGR, and low Apgar scores at birth.
- Associated with intracranial hemorrhage and necrotizing enterocolitis; cardiac, skull, and genitourinary malformations; and ↑ incidence of sudden infant death syndrome (SIDS).
- Cocaine withdrawal in an infant causes irritability, ↑ tremulousness, and poor feeding, as well as ↑ incidence of learning difficulties and attention and concentration deficits later on.

Narcotics

Heroin and methadone are associated with IUGR, SIDS, and infant narcotic withdrawal syndrome.

Tobacco

Smoking is associated with ↓ birth weight.

Phenytoin

Phenytoin is associated with **fetal hydantoin syndrome,** which includes IUGR, mental retardation, dysmorphic facies, and hypoplasia of nails and distal phalanges.

Tetracycline

Tetracycline causes tooth discoloration and inhibits bone formation.

Isotretinoin (Accutane)

Accutane is associated with hydrocephalus, microtia, micrognathia, and aortic arch abnormalities.

Warfarin

- Warfarin causes abnormal cartilage development, mental retardation, deafness, and blindness.
- Warfarin is no longer used in pregnant women due to the advent of low-molecular-weight heparin, which has fewer side effects and is well tolerated.

Maternal Conditions

DIABETES

- Associated with macrosomia (weight >4 kg), which can → birth-related injury.
- Fetal complications are related to degree of control of maternal diabetes.
- Other fetal/neonatal complications include metabolic disorders (hypoglycemia, hypocalcemia, and hypomagnesemia), perinatal asphyxia, respiratory distress syndrome, hyperbilirubinemia, polycythemia and hyperviscosity, and congenital malformations including cardiac, renal, gastrointestinal, neurologic, and skeletal defects.

WARD TIP

Cocaine use is associated with placental abruption.

WARD TIP

Infants of narcotic-abusing mothers should never be given naloxone in the delivery room because it may precipitate seizures.

EXAM TIP

Elevation of maternal glucose causes elevated fetal glucose, → fetal hyperinsulinism, which can → hypoglycemia in the newborn.

EXAM TIP

Vascular disease of placenta, caused by maternal illness (such as diabetes or lupus) can → insufficient supply of nutrients to fetus and IUGR.

OTHERS

- Hypertension and renal and cardiac disease are associated with small-for-gestational-age babies and prematurity.
- Maternal lupus is related to first-degree atrioventricular (AV) block in affected infants.

Delivery Room

DELIVERY ROOM CARE

- Once the head is delivered, the nose and mouth are suctioned.
- Once the whole body is delivered, the newborn is held at the level of the table and the umbilical cord is clamped.
- Newborn is then placed under radiant warmer and is dried with warm towels.
- Mouth and nose are gently suctioned if needed.
- Gentle rubbing of the back or flicking of the soles of the feet, if needed, to stimulate breathing.
- When the umbilical cord is clamped and cut, absent blood flow within the umbilical vein → the closure of the ductus venosus.

APGAR SCORING

- Practical method of assessing newborn infants immediately after birth to help identify those requiring resuscitation on a scale of 0–10. It is not a substitute for assessing the ABCs in neonatal resuscitation.
- Apgar scores do not predict the overall outcome of the baby in the immediate post-natal period.
- Assessment at 1 and 5 minutes; further assessments at 10 and 15 minutes may indicate success of resuscitation (see Table 2-3). Resuscitation efforts should not be delayed or interrupted to assign an Apgar score.
- A poor Apgar score alone cannot be used to diagnose asphyxia or predict the development of cerebral palsy.

TABLE 2-3. Apgar Scoring

	ACTIVITY (MUSCLE TONE)	PULSE	GRIMACE (REFLEX IRRITABILITY)	APPEARANCE (SKIN COLOR)	RESPIRATION
0	Absent	Absent	No response	Blue-gray, pale all over	Absent
1	Arms and legs flexed	Below 100 bpm	Grimace	Normal, except for extremities	Slow, irregular
2	Active movement	Above 100 bpm	Sneeze, cough, pull away	Normal all over	Good crying

Total out of 10: 7–10 normal newborn; 4–7 may require some resuscitative measures; ≤ 3 require immediate resuscitation.

- Gonococcal and chlamydial eye infection prophylaxis is with erythromycin or tetracycline ointment.
- Vitamin K is given intramuscularly (IM) to prevent hemorrhagic disease of the newborn.

CORD BLOOD/STEM CELLS

- Blood gas study should be sent if fetal distress is present.
- Can be used to test for infant's blood type.
- Rich in stem cells, which are pleuripotential cells that have potential use in malignancies and gene therapy.

Nursery Exam

GENERAL APPEARANCE

Plethora (high hematocrit secondary to chronic fetal hypoxia), jaundice, sepsis and TORCH infections, cyanosis (with congenital heart and lung disease), pallor (anemia, shock, patent ductus arteriosus).

SKIN

- Erythema toxicum is a pustular rash distributed over the trunk, face, and extremities, which resolves over a week.
- Mongolian spots (gray slate lesions) are bluish spots present over the buttocks and back that are seen in infants of African, Asian, and Native American descent that tend to fade over a year.
- Capillary hemangiomas ("stork bites") are pink spots over the eyelids, forehead, and back of the neck that tend to fade with time.
- See Dermatologic Disease chapter.

HEAD

- Anterior fontanelle closes at 9–12 months.
- Large fontanelle is seen in hypothyroidism, osteogenesis imperfecta, and some chromosomal abnormalities.
- Absent anterior fontanel is associated with craniosynostosis.

FACE

- Mouth—look and feel for cleft lip/palate and macroglossia (large tongue is seen with hypothyroidism, Down Syndrome, and Beckwith-Wiedemann syndrome).
- Coarse facial features are associated with mucopolysaccharidoses.
- Look for dysmorphic features, including micrognathia, bossing of the forehead, hypertelorism (widely spaced eyes), and low-set ears (Down syndrome) (see Congenital Malformations and Chromosomal Abnormalities chapter).

EYES

- Check for red reflex with ophthalmoscope. An absent red reflex in one or both eyes signifies blockage of the passageway between the cornea and retina such as associated with cataracts or eye tumor (retinoblastoma).

FIGURE 2-4. **Head CT consistent with TORCH infection—marked ventricular dilation, extensive encephalomalacia involving both cerebral hemispheres, absent corpus callosum, periventricular calcifications, skull deformity with overriding sutures.**

- Look for cataracts, Brushfield spots (salt-and-pepper speckling of the iris seen in Down syndrome), leukocoria (white pupil) with retinoblastoma (rare), and subconjunctival hemorrhage, which can occur after a traumatic delivery.
- See Special Organs—Eye, Ear, Nose chapter.

NECK

- Inspect for thyroid enlargement and palpate along the sternocleidomastoid for hematoma.
- Check for any fistula or tracts, which are associated with branchial closure malformations.

CHEST

- Symmetry/equality of breath sounds.
- Retractions, grunting, and tachypnea may signify respiratory distress (nasal flaring, intercostal retractions, use of accessory muscles).
- Breasts may be enlarged from the effects of maternal estrogens.

CARDIOVASCULAR

- Heart rate rhythm, quality of heart sounds, and the presence of a murmur. Murmur in a newborn infant can be due to open ductus arteriosus, but persistent murmur is always pathologic and needs evaluation.
- Check pulses and compare brachial with femoral pulse to get an estimate of vascular volume and also to rule out aortic arch obstruction (aortic stenosis, coarctation of aorta), where the femoral pulses will be weak or absent.

ABDOMEN

- Palpate for masses.
- Examine umbilicus for omphalocele and gastroschisis.
- Inspect the umbilical cord for single umbilical artery (normally two); if present, may indicate congenital anomalies, especially renal abnormalities.

EXTREMITIES

- Check both clavicles for any step off especially in the midclavicular area, where most clavicles fractures occur. Also assess for crepitus.
- Primitive reflexes (see Growth and Development chapter).
- Examine for congenital hip dysplasia with Ortolonia and Barlow.

BACK

Look for dimples or tufts of hair that may indicate spina bifida.

GENITALIA

- Girls may have vaginal bleeding and swollen labia secondary to withdrawal of maternal estrogens.
- In boys, palpate for the presence of testicles in scrotum and look for hypo- or epispadias (urethral opening proximal to normal position either on the dorsal or ventral surface).
- Examine anal opening and tone to assess for possibility of imperforate anus.

WARD TIP

Acrocyanosis (blue hands and feet only) can be normal in a newborn.

WARD TIP

Papilledema does not occur in infants with open cranial sutures.

Small or Large for Gestational Age

SMALL FOR GESTATIONAL AGE (SGA)

- Birth weight less than the tenth percentile for gestational age.
- There are two broad categories, early and late onset.
- Early onset:
    - Insult that begins before 28 weeks' gestational age.
    - Head circumference and height are proportionally small-sized **(symmetric).**
    - Seen in infants born to mothers with severe vascular disease with hypertension, renal diseases, congenital anomalies, infections, and chromosomal abnormalities.
- Late-onset or **asymmetric** IUGR.
    - Occurs with an insult after 28 weeks' gestational age.
    - Sparing of the head circumference.
    - Can occur with multiple gestation and preeclampsia.

LARGE FOR GESTATIONAL AGE (LGA)

- Birth weight greater than the 90th percentile for gestational age.
- Those at risk are infants of diabetic mothers, postmature infants, and those with Beckwith-Wiedemann syndrome.
- Most LGA infants have large parents and are constitutionally large.
- Macrosomic infants are those with a birth weight >4 kg.

Birth Trauma

CLAVICULAR FRACTURE

- Most common bone fracture during delivery.
- Complete fracture symptoms involve ↓ or absent movement, gross deformity of clavicle, tenderness on palpation, and localized crepitus.
- Greenstick (partial) fractures have no symptoms and the diagnosis is made at 7–10 days because of callus formation.
- Management is often conservative (pin arm inside sleeve to shirt to ↓ movement).

CAPUT SUCCEDANEUM

- Area of edema over the presenting portion of the scalp during a vertex delivery.
- Associated with bruising and petechiae.
- Can cross suture lines.

CEPHALOHEMATOMA

- Caused by bleeding that occurs below the periosteum of the overlying bone (usually the parietal).
- Associated with skull fractures in 5–10%, most often linear.
- Contained within the periosteum: does not cross suture lines.

WARD TIP

Absent breath sounds may signify a tension pneumothorax or atelectasis; bowel sounds in the thorax may indicate congenital diaphragmatic hernia.

EXAM TIP

Diminished femoral pulses are seen in coarctation of the aorta.

EXAM TIP

The most common cause of an abdominal mass in a newborn is an enlarged kidney.

WARD TIP

Layers of the skull can be remembered by this mnemonic:

SCALP

Skin
Cutaneous tissue
Aponeurosis
Loose areolar tissue
Periosteum

- **Subgaleal bleed:**
    - Usually associated with delivery trauma or a bleeding disorder.
    - Always between the aponeurosis and periosteum layers, with bleeding into the loose areolar tissue.
    - Crosses suture lines and feels very boggy with localization to the dependent area.
    - Risk factor for significant indirect hyperbilirubinemia in the infant.

SKULL FRACTURE/EPIDURAL HEMATOMA

- Skull fractures are uncommon; most are linear and associated with cephalohematoma. Depressed fractures are often visible and may require surgery.
- Epidural hematomas are rare and may require prompt surgical evacuation.

MOLDING

- Temporary asymmetry of the skull from the overlapping of bones that occurs following prolonged labor and vaginal deliveries.
- Normal head shape is regained within a week.

KLUMPKE PALSY

- Involves the lower arm and affects the seventh and eighth cervical and first thoracic nerve roots. The hand is paralyzed and has an absent grasp reflex, causing a "claw hand" deformity.
- It is rare to have an isolated Klumpke palsy.
- Is often accompanied by Horner syndrome.

ERB PALSY

- Erb-Duchenne involves the upper arm and is the most common type.
- Involves the fifth and sixth cervical roots, and the arm is adducted and internally rotated, but the grasp reflex is intact (see Figure 2-5).
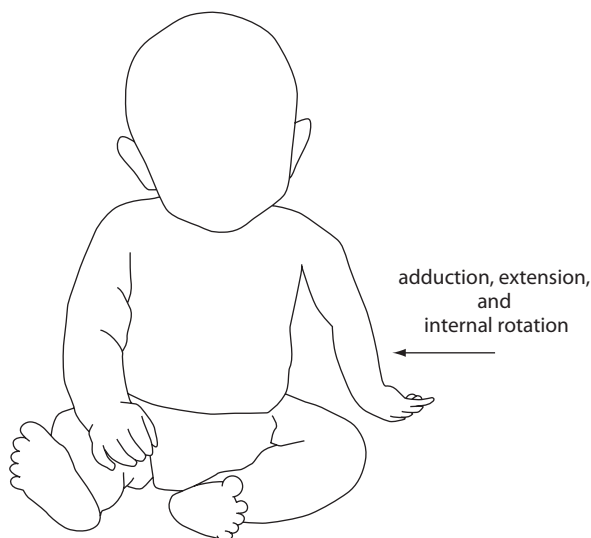

adduction, extension, and internal rotation

FIGURE 2-5. Erb palsy.

Perinatal Infections

RISK FACTORS

- Rupture of amniotic membranes for 18 hours or more.
- Chorioamnionitis. Diagnosed in the mother by the Ob-Gyn during labor and delivery.
- Intrapartum maternal fever.
- Maternal group B *Streptococcus* (GBS) colonization.
- Prematurity.
- Maternal UTI with gram-negative organisms is emerging as the common cause due to perinatal GBS prophylaxis.

GROUP B *STREPTOCOCCUS* (GBS)

- Major cause of severe systemic infection in neonates.
- Vertical transmission most important route of transmission.
- Two patterns of disease:
  - Early-onset disease: (<72 hours?)
    - Presents shortly after birth (usually <12 hours) as sepsis, pneumonia, or meningitis.
    - Infants <24 hours of age may not have fever.
    - Can be associated with persistent pulmonary hypertension of the newborn (PPHN).
  - Late-onset disease (>72 hours to 3 months): Occurs after the first week of life and most often manifests as bacteremia without a source. The most common focal infection is meningitis (35%) and presents with bulging fontanelle, lethargy (poor feeding, not waking to feed), irritability, vomiting, and seizures.
- Diagnosis is confirmed by GBS isolation from sterile body fluid (blood, cerebrospinal fluid).
- Empiric therapy with ampicillin and gentamicin should be started only if infant is symptomatic (i.e., apnea, low temperature, feeding intolerance).
- If infant is asymptomatic, monitoring for 48 hours is sufficient since infant will typically show signs of infection within a 48-hour period. Obtain CBC and blood culture.
- Intrapartum therapy with penicillin G does not prevent late-onset disease but protects against early-onset disease.

ESCHERICHIA COLI

- Principal cause of gram-negative sepsis and meningitis in newborn.
- Commonly colonize genitourinary (GU) and gastrointestinal (GI) tracts.
- Risk factors include maternal urinary tract infection (UTI) during last month of pregnancy in addition to previously mentioned risk factors.
- Clinical manifestations include sepsis, meningitis, UTI, pneumonia.
- Diagnosis is confirmed by *E. coli* isolation from normally sterile body fluids.
- Treatment should be based on antibiotic sensitivity data, but a third-generation cephalosporin should be used as an empiric agent.
- *E. coli* infection in the infant is common in infants with galactosemia.

LISTERIA MONOCYTOGENES

- Important cause of neonatal sepsis.
- Colonizes GU tract.

WARD TIP

Degree of functional return in birth brachial plexus injuries depends on the severity of the nerve injury (stretch, rupture, avulsion).

WARD TIP

Twenty percent of pregnant women are colonized with GBS. It is recommended that all pregnant women be screened (vaginal, rectal swabs) at 35–37 weeks of gestation, and be given intrapartum antibiotics if positive.

- Clinical manifestations include sepsis and meningitis.
- Diagnosis is confirmed by *L. monocytogenes* isolation from sterile body fluid.
- Treatment is with penicillin or ampicillin.

HERPES SIMPLEX

- Prevalence rate for adults with genital herpes is about 20%.
- Risk of neonatal disease is much higher with primary maternal infection (44%), and only 3% for a recurrent one.
- Ninety percent of neonatal infection is acquired through infected secretions during birth.
- There are three distinct patterns of disease:
  - Cutaneous disease:
    - Involves skin, mouth, and eyes.
    - Vesicular eruptions appear around 7–10 days of life, usually on presenting part.
    - If not recognized promptly, can progress to disseminated disease.
  - Encephalitic disease:
    - Occurs at second to third week of life.
    - Clinical signs include lethargy, irritability, poor suck, seizures.
    - Cutaneous lesions may be absent.
  - Disseminated disease:
    - Sepsis-like clinical picture (apnea, irritability, hypotonia, hypotension).
    - Cutaneous lesions may be absent.

> **EXAM TIP**
>
> Cesarean section is performed for women with primary genital herpes and vaginal lesions in late gestation.

DIAGNOSIS

- HSV can be isolated in cell culture from skin lesions or nasopharyngeal swabs.
- Polymerase chain reaction (PCR) is a sensitive tool for HSV detection.

TREATMENT

- Acyclovir is very effective in treatment of HSV infection.
- Course of treatment is often prolonged (21 days) for encephalitic and disseminated forms.

CHLAMYDIA

A 3-week-old infant presents with paroxysmal cough and tachypnea, but no fever; bilateral diffuse crackles, hyperinflation, and patchy infiltrates on x-ray; he had conjunctivitis at 10 days of age. *Think: Chlamydia trachomatis*.

The incubation period of chlamydial conjunctivitis is between 5 and 14 days; usually manifests later than gonococcal conjunctivitis (occurs 2–5 days after birth). It is commonly acquired from the birth canal during delivery. It is the most common infectious cause of conjunctivitis in the neonates. Generally, gonococcal conjunctivitis usually has a more rapid and progressive course than *Chlamydia.*

> **EXAM TIP**
>
> Erythromycin use has been associated with development of pyloric stenosis.

- Acquired during passage through the birth canal of an infected mother.
- Causes conjunctivitis (few days to several days) and pneumonia (between 3 and 19 weeks).
- Characteristic "staccato" cough may not be evident in newborn infants, and may present with frequent apneic episodes.

DIAGNOSIS

Culture.

TREATMENT

Erythromycin orally for 14 days.

SYPHILIS

- Results from transplacental transfer of *Treponema pallidum.*
- Common features include intermittent fever, osteitis and osteochondritis, hepatosplenomegaly, lymphadenopathy, persistent rhinitis ("snuffles"), and a maculopapular rash involving the palms and the soles.
- Late manifestations include a saddle nose deformity, saber shins, frontal bossing, Hutchison teeth and mulberry molars, sensorineural, and Clutton's joints (painless joint effusions).

DIAGNOSIS

- Rapid plasma reagin (RPR) titers and the flourescent treponemal antibody-absorption test (FTA-ABS).
- Treponemes can also be seen on darkfield microscopy of nasal discharge.

TREATMENT

Penicillin G.

HIV

- Up to 25% of pediatric human immunodeficiency virus (HIV) infection results from maternal-fetal vertical transmission.
- Transmission from infected breast milk can occur; however, exclusively breast-fed infants have lower transmission rates.
- Clinical features in the infant include persistent thrush, lymphadenopathy and hepatosplenomegaly, severe diarrhea, failure to thrive, and recurrent infections.
- Strategies to reduce transmission:
  - Maternal treatment with ZDV during pregnancy.
  - Consider elective C-section at 38 weeks when feasible.
  - Mothers who are HIV positive should be advised not to breast-feed due to risk of transmission.

DIAGNOSIS

Detection of p24 antigen in peripheral blood, PCR to detect viral nucleic acid in peripheral blood, and enzyme-linked immunosorbent assay (ELISA) for the detection of antibodies.

TREATMENT

Nutritional support, *Pneumocystis jiroveci* prophylaxis, antiviral therapy, and anti-infective agents for specific infections.

Selected Problems in Full-Term Infants

DEVELOPMENTAL DYSPLASIA OF THE HIP (DDH)

- Occurs in ~1 in 800 births.
- More common in white females with breech presentation, and is more likely to be unilateral and involve the left hip.

EXAM TIP

Maternal treatment with zidovudine (ZDV) in the second trimester reduces the rate of transmission by >70%.

WARD TIP

Delivery room management of a meconium-stained infant consists of nasopharyngeal suctioning before the delivery of the thorax. Infants with respiratory depression require intubation and tracheal suctioning.

- Signs include asymmetry of the skin folds in the groin and shortening of the affected leg.
- Evaluation maneuvers:
    - Ortolani—abduction of the hips by using gentle inward and upward pressure over the greater trochanter.
    - Barlow—adduct the hips by using the thumb to apply outward and backward pressure; "clunking" of reduction and dislocation are elicited in patients with hip dislocation.
- Diagnosis is confirmed by ultrasound. Current American Academy of Pediatrics (AAP) guidelines ask for ultrasound only in female infants with breech presentation and a hip click usually performed at 6 weeks of age.
- Can be treated with a special brace (Pavlik harness) or sometimes casting. See Musculoskeletal Disease chapter.

MECONIUM ILEUS/ASPIRATION

A full-term male infant was born after a prolonged second stage of labor and thick meconium at delivery. He was depressed at birth, requiring intubation and suction of the meconium from below the vocal cords. His condition improved quickly, and he was vigorous at 3 minutes of life. Apgar score was 3 and 7 at 1 and 5 minutes of life, respectively. He was doing well in the well-baby nursery until at 3 hours of life, when he was noted to have dusky episode and was transferred to the special care nursery where his O_2 saturation was noted to be 82% breathing room air. He was placed in oxyhood oxygen climbing up to 100% with borderline O_2 saturation in the mid-80s. He was intubated and started on mechanical ventilation. His chest x-ray is shown in the figure. What is the likely diagnosis and management of this infant?

The infant described has characteristic meconium aspiration syndrome as seen by nodular appearance of both lung fields on the chest x-ray. He is developing persistent pulmonary hypertension of the newborn (PPHN), management of which includes aggressive ventilation, inhaled nitric oxide, and close monitoring of the gas exchange. An echocardiogram is useful to provide details on the elevated pulmonary pressures as well as to rule out any cardiac defects. Infants are at risk of hypotension and shunting of pulmonary flow via the ductus arteriosus into the systemic circulation resulting in differential O_2 saturation in the upper and lower extremities and require pressor support (dopamine, dobutamine, epinephrine) to elevate systemic blood pressure to the level above pulmonary pressure to prevent hypotension and shunting.

- Meconium is the first intestinal discharge of a newborn infant and is composed of epithelial cells, fetal hair, mucus, and bile.
- Intrauterine stress may cause passage of meconium into the amniotic fluid, which can cause airway obstruction and a severe inflammatory response, → severe respiratory distress known as meconium aspiration syndrome.
- Full-term and post-date infants are at higher risk for meconium aspiration.
- Meconium ileus occurs when meconium becomes obstructed in the terminal ileum; presentation is with failure to pass stool, abdominal distention, and vomiting.
- Infants with meconium ileus should be tested for cystic fibrosis.

HYPOXIC/ISCHEMIC ENCEPHALOPATHY

- Hypoxic ischemic encephalopathy is an important cause of permanent damage to the cells of the CNS that occurs secondary to hypoxia (↓ oxygen delivery) and ischemia (↓ blood flow).

- Can be caused by maternal conditions (hypertension), placental insufficiency, placental abruption, severe neonatal blood loss, and overwhelming infection.
- Neurologic manifestations include hypotonia, absent or decreased primitive reflexes, coma, and seizures.
- It can result in death, cerebral palsy (CP), and mental retardation.
- Newer modalities of treatment include selective head cooling or whole body cooling, which are used at several tertiary care neonatal intensive care units (NICUs) in the United States.

CONGENITAL DIAPHRAGMATIC HERNIA (CDH)

- Associated with chromosomal abnormalities, low birth weight, and IUGR.
- Can be diagnosed on prenatal ultrasound (between 16 and 24 weeks).
- Signs and symptoms include respiratory distress immediately on delivery, tachypnea, poor breath sounds over affected side of chest (most commonly **left**), and scaphoid abdomen.
- Prenatally diagnosed diaphragmatic hernia in a neonate warrants an ex-utero intrapartum treatment (EXIT) procedure, where neonatologists and surgeons are present at delivery and infant is intubated and central extracorporeal membrane oxygenation (ECMO) catheters placed at the delivery of the head and neck.
- Respiratory distress is a cardinal sign in neonates with CDH.

JAUNDICE

- Common causes of hyperbilirubinemia include ABO incompatibility, breast milk and breast-feeding jaundice (see Nutrition chapter), Rh iso-immunization, and infection.
- **Conjugated hyperbilirubinemia (direct):**
  - When an infant's direct (conjugated) bilirubin is >3 mg/dL or more than 20% of the total bilirubin.
  - Most common causes are idiopathic neonatal hepatitis (diagnosis of exclusion) and biliary atresia.
- **Unconjugated hyperbilirubinemia (indirect):**
  - When an infant's indirect (unconjugated) serum bilirubin level is >10 mg/dL in term infants. Nomograms developed by AAP are used to plot bilirubin levels and to categorize infants into low-, medium-, or high-risk group and need for treatment.
  - Most common cause of neonatal jaundice, seen in up to 50% of neonates.
  - Secondary to ↑ bilirubin load, defective uptake and conjugation, and impaired excretion into bile.
  - Physiologic hyperbilirubinemia is seen after the first 24 hours of life, peaks at 3 days, and resolves over 2 weeks.
- **Kernicterus:**
  - Bilirubin neurotoxicity secondary to persistently elevated bilirubin levels, which exceed albumin-binding capacity of the blood resulting in deposition of bilirubin in the basal ganglia.
  - This can result in subtle neurologic deficits, hearing loss, profound encephalopathy, and death.
- Treatment is initiated to prevent kernicterus.
  - Phototherapy with blue-green light converts bilirubin in skin to non-toxic isomers that are excreted without conjugation.
  - Elevated bilirubin levels (12–20 mg/dL) are usually treated with phototherapy.
  - Exchange transfusion should be considered at higher levels (20–25 mg/dL).

WARD TIP

Only 10% of patients with cerebral palsy have birth events associated with asphyxia; the cause of the majority of cases of CP remains unknown.

EXAM TIP

High indirect serum bilirubin levels in the first 24 hours of life are never physiologic.

WARD TIP

In neonates there is a cephalopedal progression of jaundice; approximate levels for involvement:
- Head and neck: 4–8 mg/dL
- Upper trunk: 5–12 mg/dL
- Lower trunk and thighs: 8–16 mg/dL
- Arms and lower legs: 11–18 mg/dL
- Palms and soles: >15 mg/dL

Newborn Screening

NEONATAL SCREENING

- Available for various genetic, metabolic, hematologic, and endocrine disorders.
- All states have screening programs, although specific tests required vary.
- Tests performed on heel puncture include those for hypothyroidism, galactosemia, adrenal hyperplasia, cystic fibrosis, phenylketonuria, and other organic acid and aminoacidopathies.

AUDITORY SCREENING

- Hearing impairment can affect speech and language development and occurs in 5 in 1000 births.
- All infants should be screened with otoacoustic emission hearing testing.

EXAM TIP

Early diagnosis of hypothyroidism and treatment with thyroid hormone prior to 3 months of age can greatly improve intellectual outcome.

HIGH-YIELD FACTS IN

Prematurity

Prematurity

DEFINITIONS

- Premature infant: Live-born newborn delivered prior to 37 weeks' gestation.
- Low birth weight (LBW): <2500 g.
- Very low birth weight (VLBW): <1500 g.
- Extremely low birth weight (ELBW): <1000 g.
- Extremely low gestational age neonate (ELGAN): <28 weeks' gestation.

ETIOLOGY

- Most premature births have no identifiable causes.
- Identifiable contributors include maternal, fetal, and obstetric:
    - Maternal:
        - Low socioeconomic status.
        - Preeclampsia.
        - Infections (urinary tract infections, group B streptococcus, etc).
        - Chronic medical illness (hypertension, renal disease, diabetes, cyanotic heart disease, etc).
        - Drug use.
    - Fetal:
        - Multiple gestation.
        - Fetal distress (from hypoxia, etc).
        - Congenital anomalies.
    - Obstetric:
        - Cervical Insufficiency.
        - Polyhydramnios.
        - Chorioamnionitis.
        - Premature rupture of membranes.
        - Placenta previa and abruptio placenta.

EXAM TIP

Placing a healthy premature neonate in a neutral thermal environment reduces calories burned.

Common Problems in Premature Newborns

RESPIRATORY DISTRESS SYNDROME (RDS; HYALINE MEMBRANE DISEASE OF THE NEWBORN)

ETIOLOGY/PATHOPHYSIOLOGY

- Immature lung structure; alveoli are small, inflate with difficulty, and do not remain gas-filled between inspirations.
- Occurs secondary to insufficiency of lung surfactant due to immaturity of surfactant producing type 2 alveolar cells.
- Surfactant quality and quantity increases as fetus nears term. The greatest risk for RDS is in infants less than 34 weeks.
- High surface tension and propensity for alveolar collapse.
- Alveolar collapse results in progressive atelectasis, intrapulmonary shunting, hypoxemia, and cyanosis.
- Rib cage is weak and compliant.

EPIDEMIOLOGY

- Usually seen in infants <32 weeks' gestational age, but has been seen in full-term infants, especially when the mother has maternal diabetes.
- The incidence of RDS is inversely proportional to gestational age.

EXAM TIP

Production of surfactant can be accelerated by maternal steroid (betamethasone) administration; best if given 24–48 hours prior to delivery. Every woman at increased risk of delivery before 34 weeks should be given betamethasone if possible.
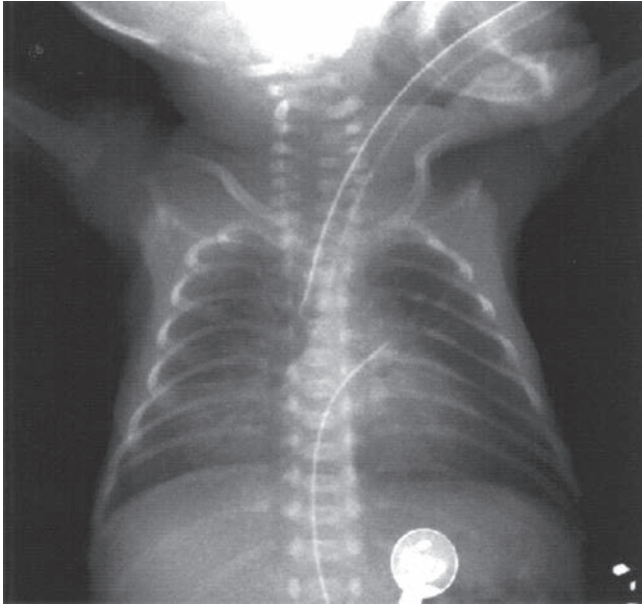
FIGURE 3-1.   Chest x-ray demonstrating "ground glass" infiltrates consistent with respiratory distress syndrome (with a more focal area of infiltrate or atelectasis in the medial right lung base).

SIGNS AND SYMPTOMS

- Usually seen within the first 4 hours of life.
- Tachypnea.
- Grunting and nasal flaring.
- Retractions.
- Cyanosis.

DIAGNOSIS

Chest x-ray with fine, diffuse reticulogranular or "ground glass" pattern and air bronchograms (see Figure 3-1).

TREATMENT

- Respiratory support, including oxygen, continuous positive airway pressure (CPAP), intubation, and mechanical ventilation.
- Exogenous surfactant replacement (instillation via endotracheal tube) has dramatically reduced mortality in infants with RDS.

BRONCHOPULMONARY DYSPLASIA (BPD)

DEFINITION

- Chronic lung disease that develops in preterm neonates treated with oxygen and positive-pressure ventilation.
- Diagnosed by the need for supplemental oxygen beyond 28 days of life or at 36 weeks postmenstrual age.
- Characterized by decreased septation and alveolar hypoplasia leading to reduced surface area, with abnormal capillary development that increases pulmonary resistance.

ETIOLOGY

- Multifactorial.
- Lung immaturity.

> **WARD TIP**
>
> Most of these neonates also receive antibiotics because clinically and radiographically RDS and congenital pneumonia are indistinguishable.

- Prolonged mechanical ventilation leading to barotrauma and volutrauma.
- Oxygen toxicity to the lungs.
- Infection (sepsis, chorioamnionitis).

SIGNS AND SYMPTOMS

- Tachypnea.
- Retractions.
- Wheezing or rales.

DIAGNOSIS

Chest x-ray with air-trapping, atelectasis, and/or pulmonary edema. Severe BPD may show hyperinflation.

TREATMENT

- Supplemental oxygen as needed with gradual weaning over 2–4 months.
- Inhaled or oral steroids.
- Bronchodilators.
- Diuretics.

NECROTIZING ENTEROCOLITIS (NEC)

A 32-week-gestation female infant was doing well and advanced to full enteral feeds at 14 days of life. At day 15 of life she was noted to have significant abdominal distention and bloody stools. X-ray of the abdomen is shown in the figure. What is the likely diagnosis and management of the condition shown in this x-ray?

X-ray of this infant is consistent with necrotizing enterocolitis with evident pneumatosis intestinalis (free air within the bowel wall) in the descending colon area. Management includes serial x-rays to detect perforation of the bowel wall, which requires immediate surgery to seal the bowel. Medical management before perforation includes NPO, IV fluids, and IV antibiotics for a period of 14 days.

The most common gastrointestinal emergency in premature infants.

ETIOLOGY

- Seen primarily in premature infants, but can occur in full-term neonates.
- Incidence and mortality are inversely related to gestational age and birth weight.
- Pathogenesis is unknown, but most likely a multifactorial etiology including bowel wall ischemia and bacterial invasion.
- Spontaneous intestinal perforation is more common in premature infants treated with indomethacin for patent ductus arteriosus. Indomethacin may cause splanchnic vasoconstriction.

SIGNS AND SYMPTOMS

- Intolerance of oral feeding (vomiting, bilious aspirates).
- Change in behavior (lethargy).
- Abdominal distention and/or tenderness, abdominal skin discoloration.
- Bradycardia.
- Temperature instability.
- Respiratory distress. Increased episodes of apnea and desaturation, respiratory failure.
- Metabolic acidosis, sepsis, shock.
- Lab values (low or high WBC, thrombocytopenia, glucose dysregulation).

FIGURE 3-2.   Necrotizing enterocolitis.

DIAGNOSIS

- Distended loops of bowel.
- Abdominal x-ray with "pneumatosis intestinalis"—air bubbles within the bowel wall (see Figure 3-2) is the hallmark radiographic finding for NEC.
- Air in portal vein.
- Free air in the abdomen (in case of perforation).
- Occult/frank blood per rectum.

TREATMENT

- NPO.
- Nasogastric decompression.
- Intravenous fluids (for volume resuscitation and total parenteral nutrition).
- Blood cultures followed by treatment with broad-spectrum antibiotics with anaerobic coverage.
- Surgery as needed (bowel necrosis, intestinal perforation, pneumoperitoneum, failure of medical treatment).

RETINOPATHY OF PREMATURITY (ROP)

Disease that affects immature vasculature in the eyes of premature infants.

ETIOLOGY

- Caused by abnormal proliferation of immature retinal vessels.
- Abnormal vessels can lead to retinal detachment and blindness in severe cases.
- Incidence and severity are inversely related to gestational age and birth weight.

WARD TIP

An absolute indication for operative intervention in NEC is pneumoperitoneum indicating bowel perforation.

WARD TIP

Currently, severe retinopathy of prematurity is rare due to judicious use of oxygen.

EXAM TIP

All infants <1500 g birth weight or younger than 30 weeks' gestational age at birth are at risk of developing ROP.

- Pathogenesis: 1. Injury to developing vasculature (risk factors include hyperoxia, hypoxia, hypotension). 2. Subsequent abnormal new vessel development.

DIAGNOSIS

- An ophthalmology evaluation is necessary in all infants ≤1500 g or gestational age of <30 and infants with birth weight 1500–2000 g or with an unstable clinical course
- First screening exam:
    - Postmenstrual age of 30 weeks for infants born at <27 weeks of gestational age.
    - 4 weeks of chronologic age for infants >27 weeks' gestational age.

TREATMENT

- Treatment depends on severity.
- Multiple modalities are available: laser photocoagulation, cryotherapy, and anti-VEGF agents.

INTRAVENTRICULAR HEMORRHAGE (IVH)

DEFINITION

- Rupture of germinal matrix blood vessels due to:
    - Germinal matrix fragility because of immaturity.
    - Fluctuations in cerebral blood flow: hypoxic-ischemic injury, increased arterial blood flow, or increased venous pressure.
- Most IVHs occur within 72 hours after birth.

PREDISPOSING FACTORS

- Prematurity.
- RDS.
- Hypo- or hypervolemia.
- Shock.
- Bleeding disorders.

SIGNS AND SYMPTOMS

- 25–50% of cases are asymptomatic.
- May present with fluctuating nonspecific findings over days: altered level of consciousness, hypotonia, decreased movements, changes in eye positioning or movement, disruption of respiratory function (apnea).
- Catastrophic presentation is least common and progress rapidly (stupor, coma, respiratory abnormalities, decerebrate posturing, seizures, flaccid weakness, cranial nerve abnormalities, bulging fontanelle, hypotension, bradycardia, falling hematocrit, metabolic acidosis and inappropriate ADH secretion).

DIAGNOSIS

- All infants <30 weeks of gestation should be screened at 7–14 days of chronological age and again at 36–40 weeks of postmenstrual age.
- Cranial ultrasound (through anterior fontanelle).
- Grade I: bleeding into the germinal matrix.
- Grade II: IVH in </= 50% of lateral ventricle volume.
- Grade III: IVH in >50% of lateral ventricle volume.
- Grade IV: large IVH with hemorrhagic infarction of periventricular white matter.

COMPLICATIONS

- Post-hemorrhagic hydrocephalus.
- Cerebral palsy.
- Seizures.
- Developmental delay.

TREATMENT

- Directed toward correction of underlying conditions (RDS, shock, etc).
- In cases of associated hydrocephalus, placement of ventriculoperitoneal shunt may be required.
- Prognosis is dependent on the grade of IVH:
- Grades I and II: Good outcome.
- Grade III: Significant cognitive impairment.
- Grade IV (periventricular hemorrhage infarction): Major neurologic problems and almost 40% mortality.

SURVIVAL OF PREMATURE NEONATES

- Disorders related to prematurity and low birth weight are the leading cause of neonatal death.
- There is no worldwide, universal gestational age that defines viability.
- Survival rates in developed countries: 15% for babies <500 g, 60% for babies between 500 and 750 g, >90% for babies between 1250 and 1500 g.
- In the United States, chance of survival is 60% for babies <28 weeks' gestation.

SPECIAL CONSIDERATIONS FOR PREMATURE NEONATES

- Thermoregulation: increased susceptibility to heat loss (high body surface area-to-body weight ratio, decreased brown fat stores, non-keratinized skin, and decreased glycogen supply).
- Glucose regulation: susceptible to hypoglycemia and hyperglycemia.
- Fluid and electrolyte imbalances.
- Hyperbilirubinemia.
- Nutritional support: Ex-preemies require a specialized high-calorie diet to allow for optimized growth.
- Routine vaccination should be given based on postnatal (not gestational) age.
- Early identification and intervention is needed for infants with developmental problems.

WARD TIP

Ex-preemies can receive RSV prophylaxis with RSV monoclonal antibodies during RSV season (IM injections once a month).

WARD TIP

Premature infants have proportionally more fluid in the extracellular fluid compartment than the intracellular compartment and are at risk for fluid and electrolyte imbalance.

WARD TIP

Optimal parenteral nutrition can be achieved by total parenteral nutrition (TPN)—specialized solution consisting of amino acids, dextrose, minerals, and electrolytes.

WARD TIP

Breast milk is the best choice for enteral feeding for premature infants.

NOTES

HIGH-YIELD FACTS IN

Growth and Development

Growth

- Understanding normal growth patterns of childhood is important because it is an indication of the overall health of a child.
- Growth is influenced by both genetics and environment.

GROWTH CHARTS

- Height, weight, and head circumference are plotted on growth curves to compare the patient to the population.
- Growth charts compare individual children with the 5th, 10th, 25th, 50th, 75th, 90th, and 95th percentiles.
- **WHO vs CDC growth charts:**
  - The WHO growth standard charts consider the effect of infant feeding on growth by using breastfeeding as the norm.
  - CDC growth reference charts were developed to represent all infants in the United States. Feeding criteria were not identified.

As a result, the CDC growth charts may not adequately reflect the current growth patterns of infants in the United States. They also do not reflect the growth pattern typically seen in breastfed infants.

- Serial plotting of a patient's growth allows the clinician to observe patterns of growth over time.
- Body mass index (BMI) is plotted on growth curves for males and females from 2 to 20 years of age. BMI above 85% classifies as overweight and above 95% as obese.
- Potential limitations of particular growth charts include possible development from small population sizes, ethnic differences, and whether they represent growth potential versus proper care and feeding.
- Specialized charts exist for children who are premature (Babson), have Down syndrome, myelomeningocele, Prader-Willi syndrome, cerebral palsy, or Williams syndrome.

EARLY GROWTH TRENDS

- A term infant, who is breast-feeding, regains birth weight by 2 weeks. A formula-fed infant usually regains birthweight by 10 days.
- During the first 3 months, a child is expected to gain 20 to 30 g/day or close to 1 kg/month.
- A child doubles birth weight by the fifth month of life and triples by his or her first birthday.
- Growth chart recording should be adjusted for gestational age until the infant is 2 years old.
- Normal growth from birth to 6 months is 1.5–2.5 cm/month. Between 6 and 12 months, 1 cm/month.
- Children with genetic short stature may have normal length and weight at birth but their growth percentiles decline within the first 2–3 years.
- Appetite normally ↓ in the second year of life coincident with the slowing of the growth rate.

INTRAUTERINE FACTORS

- Insulin-like growth factor (IGF) is important for fetal growth.
- Growth hormone and IGF are both important for postnatal growth.

- Thyroid hormone is important for central nervous system (CNS) development, but not important for fetal growth.
- Fetal weight gain is greatest during the third trimester.
- Teratogens, TORCH infections (toxoplasmosis, other [hepatitis B, syphilis, varicella-zoster virus], rubella, cytomegalovirus, herpes simplex virus/human immunodeficiency virus), and chromosomal abnormalities (trisomy 21, Turner syndrome) can impair fetal growth. Smoking during pregnancy can lead to a low birthweight.

TEETH

- By age 2½, children should have all of their primary teeth including their second molars.
- Central incisors are first to erupt, between 6 and 12 months.
- Second molars are last to erupt, between 23 and 33 months.
- Secondary (permanent) teeth begin to erupt by age 6–7 years.
- Early or late tooth eruption may be within normal limits, though it can be an indicator of a nutritional, genetic, or metabolic problem.
- Delayed eruption:
    - Endocrine disorders (hypothyroidism).
    - Genetic abnormalities (Down syndrome).

Specific Growth Problems

MICROCEPHALY

DEFINITION

The definition of microcephaly is not standardized. It is sometimes defined as an occipitofrontal circumference (OFC) more than 3 standard deviations (SD) below the mean for a given age, sex, and gestation. Other times, it is defined as an OFC more than 2 SD below the appropriate mean (i.e., less than the third percentile).

ETIOLOGY

- Genetic (familial, isolated).
- Syndromic:
    - Chromosomal: Trisomy 21, 13, 18.
    - Contiguous gene deletion: Cri-du-chat syndrome, Williams syndrome.
    - Single-gene defects: Cornelia de Lange syndrome, Smith-Lemli-Opitz syndrome.
- Prenatal insults (radiation, alcohol, hydantoin, TORCH infections, maternal phenylketonuria [PKU] and maternal diabetes, ↓ placental blood flow), Zika virus.
- Perinatal hypoxic-ischemic encephalopathy.
- Structural malformation (e.g., lissencephaly),

IMPACT

When a child has **microcephaly**, the brain develops abnormally. A small brain predisposes to impaired cognitive development, delayed motor functions and speech, and seizures.

MACROCEPHALY

DEFINITION

Head circumference >3 standard deviations above the mean.

> **EXAM TIP**
>
> Measure parents' and siblings' head circumference to check for familial cause of microcephaly.

> **EXAM TIP**
>
> Weight is affected first in FTT, followed by height and head circumference.

> **EXAM TIP**
>
> Psychosocial reasons account for most cases of FTT in the United States.

ETIOLOGY

- Familial in 50% of cases.
- Hydrocephalus.
- Other causes: Large brain (megalencephaly), cranioskeletal dysplasia, Sotos syndrome.

FAILURE TO THRIVE (FTT)

DEFINITION

FTT is defined as a weight below the third percentile or a fall off the growth chart by two percentiles.

ETIOLOGY

- Organic causes include disease of any organ system.
- Nonorganic causes include abuse, neglect, and improper feeding (see Table 4-1).

SIGNS AND SYMPTOMS

- Expected age norms for height and weight not met.
- Hair loss.
- Loss of muscle mass.
- Subcutaneous fat loss.
- Dermatitis.
- Lethargy.
- Recurrent infection.
- Kwashiorkor—protein malnutrition.
- Marasmus—inadequate nutrition.

DIAGNOSIS

- Detailed history:
  - Gestation, labor, and delivery.
  - Neonatal problems (feeding or otherwise).
  - Breast-feeding mother's diet and medications.
  - Types and amounts of food, who prepares and how the formula or food is prepared, who feeds.
  - Vomiting, diarrhea, infection.
  - Sick parents or siblings.
  - Major family life events/chronic stressors.
  - Travel outside the United States.
  - Any injuries to child.
- Observation of parent–child interactions, especially at feedings, is critical for diagnosis.
- Lack of weight gain after adequate caloric feedings is characteristic of non-organic failure to thrive.
- Screening tests for common causes include complete blood count (CBC), electrolytes, blood urea nitrogen (BUN), creatinine, and albumin and thyroid-stimulating hormone.

TREATMENT

- If a nonorganic cause is suspected or the child is severely malnourished, hospitalization may be required.
- If organic, treat the cause.

PROGNOSIS

FTT during the first year of life has a poor outcome due to the rapid growth of the brain during the first 6 months.

WARD TIP

Signs of FTT:
SMALL KID

Subcutaneous fat loss
Muscle atrophy
Alopecia
Lagging behind norms
Lethargy
Kwashiorkor/marasmus
Infection
Dermatitis

WARD TIP

Organic versus nonorganic FTT is best distinguished by a detailed history and physical exam.

T A B L E   4 - 1 .   Etiology of FTT

Gastrointestinal

Nutritional

- Kwashiorkor
- Marasmus
- Zinc/iron deficiency

Feeding Disorder

- Oral-motor apraxia
- Cleft palate
- Dentition disorder

Vomiting

- Gastrointestinal reflux
- Structural anomalies
- Pyloric stenosis
- Central nervous system (CNS) lesions
- Hirschsprung disease

Diarrhea

- Chronic toddler diarrhea
- Milk protein allergy/intolerance
- Infectious
  - Bacterial
  - Parasitic
- Malabsorption
  - Cystic fibrosis
  - Celiac disease
  - Inflammatory bowel disease

Pulmonary

- Tonsillar hypertrophy
- Cystic fibrosis
- Bronchopulmonary dysplasia
- Asthma
- Structural abnormalities
- Obstructive sleep apnea

Renal

- Chronic pyelonephritis
- Renal tubular acidosis
- Fanconi syndrome
- Chronic renal insufficiency
- Urinary tract infection
- Diabetes insipidus

Endocrine

- Hypothyroidism
- Rickets
- Vitamin D deficiency
- Vitamin D resistance
- Hypophosphatemia
- Growth hormone resistance/deficiency
- Adrenal insufficiency/excess
- Parathyroid disorders
- Diabetes mellitus

CNS

- Pituitary insufficiency
- Diencephalic syndrome
- Cerebral palsy
- Cerebral hemorrhages
- Degenerative disorders

Congenital

- Inborn errors of metabolism
- Trisomy 13, 18, 21
- Russell-Silver syndrome
- Prader-Willi syndrome
- Cornelia de Lange syndrome
- Perinatal infection
- Fetal alcohol syndrome

Other

- Prematurity
- Oncologic disease/treatment
- Immunodeficiency
- Collagen vascular disease
- Lead poisoning

Nonorganic Causes

- Child neglect/abuse
- Poverty
- Lack of true caregivers
- Mental illness within the family
- Marital discord/spousal abuse in the home

Hepatic

- Chronic hepatitis
- Glycogen storage disease

Infectious

- Tuberculosis
- HIV

Cardiac

- Congenital heart malformations

Development

A child smiles spontaneously, babbles, sits without support, reaches, and feeds herself a cookie but has no pincer grasp. What is her approximate age? *Think: 8–9 months* (immature pincer grasp at 10 months). Fine pincer grasp of an object between the thumb and forefinger generally develops at 12 months of age.

- Attainment of developmental milestones is an indicator of a child's overall neurologic function.

- Maturation of intellectual, social, and motor function should occur in a predictable manner.
- It is essential that the physician recognize normal patterns in order to identify deviations.

DEVELOPMENTAL MILESTONES

- Each new motor, language, and social skill should be acquired during an expected age range in a child's life.
- Each new skill is built on an earlier skill, and skills are rarely skipped (see Table 4-2).

T A B L E 4 - 2 . Developmental Milestones

AGE	MOTOR	LANGUAGE	SOCIAL	OTHER
1 month	Reacts to pain	Responds to noise	Regards human face Establishes eye contact	
2 months	Eyes follow object to midline **Head up prone**	Vocalizes Coos by 3 months	Social **smile** Recognizes parent	
4 months	Eyes follow object past midline **Rolls over**	**Laughs and squeals**	**Regards hand**	
6 months	**Sits well unsupported** Transfers objects hand to hand (switches hands) **Rolls prone to supine**	**Babbles**	Recognizes strangers	6abbles (babbles) Six strangers switch sitting at six months
9 months	**Pincer grasp, immature (10 months)** **Crawls** Cruises (walks holding furniture)	Mama/dada, nonspecific Bye-bye	Starts to explore Stranger anxiety	Can crawl, therefore can explore It takes 9 months to be a "mama" Pinches furniture to walk
12 months	**Walks with one hand held** Throws object	Mama/dada specific and knows **1–3 words** **Follows one-step command with gesture**		Walking away from mom causes anxiety Knows 1 word at 1 year
2 years	**Walks up and down stairs** Copies a line **Runs** **Kicks ball**	**2–3-word phrases** One half of speech is understood by strangers Refers to self by name **Pronouns**	Parallel play	Puts 2 words together at 2 At age 2, ¾ (½) of speech understood by strangers

T A B L E   4 - 2 .   **Developmental Milestones (*continued*)**

AGE	MOTOR	LANGUAGE	SOCIAL	OTHER
3 years	**Copies a circle** **Pedals a tricycle** Can build a bridge of 3 cubes Repeats 3 numbers	Speaks in sentences Three fourths of speech is understood by strangers Recognizes 3 colors	Group play **Plays simple games** Knows gender Knows first and last name	*Tricycle*, 3 cubes, 3 numbers, 3 colors, 3 kids make a group At age 3, ¾ of speech understood by strangers
6 years	Draws a person with 6 parts Ties shoes	Identifies left and right		At 6 years: skips, shoes, person with 6 parts
4 years	Identifies body parts Copies a cross Copies a square (4.5 years) **Hops on one foot**	Speech is completely understood by strangers Uses past tense **Tells a story**	Plays with kids, social interaction	Song "head, shoulder, knees, and toes," 4 parts reminds you that at age 4, can identify 4 body parts
4 years	**Throws overhand**			At age 4, ¾ of speech is understood by strangers When using past tense, speaks of things that happened *before* If a 2-year-old can copy one line, a 4-year-old can copy two lines to draw a cross and a square, which has 4 sides
5 years	Copies a triangle Catches a ball Skips with alternating feet Partially dresses self	Writes name Counts 10 objects		

NEUROLOGIC DEVELOPMENT

- Myelination of the nervous system begins midgestation and continues until 2 years of age.
- Myelination occurs in an orderly fashion, from head to toe (cephalo-caudal).
- Brain at birth weighs approximately 10% of the newborn's body weight (adult brain, 2% of body weight).
- Primitive reflexes are present after birth and diminish by 6 months (see Table 4-3).

AGE ADJUSTMENT FOR PRETERM INFANTS

- Preterm infants may differ from full-term infants with regard to development.
- Age correction should be done until the child is 24 months old for children born more than 2 weeks early.
- Use the corrected age when assessing developmental progress and growth.

WARD TIP

For age adjustment between birth and 2 years, subtract the number of weeks of prematurity from the chronological age. For an 18-month-old baby who is an ex-preemie at 30 weeks, the difference from full term at 40 weeks is 10 weeks, so the corrected age is 18 months minus 10 weeks = 15½ months.

TABLE 4-3. Primitive Reflexes

REFLEX	TIMING	ELICIT	RESPONSE
Moro	Birth to 5–6 months	While supine, allow head to suddenly fall back approximately 3 cm	Symmetric extension and adduction, then flexion, of limbs
Startle	Birth to 5–6 months	Startle	Arms and legs flex immediately
Galant	Birth to 2–6 months	While prone, stroke the paravertebral region of the back	Pelvis will move in the direction of the stimulated side
Sucking	Becomes voluntary at 3 months	Stimulate lips	Sucks
Babinski	Birth to 4 months	Stroke from toes to heel	Fanning of toes
Tonic neck	Birth to 6–7 months	While supine, rotate head laterally	Extension of limbs on chin side, and flexion of limbs on opposite side (fencing posture)
Rooting	Less prominent after 1 month	Stroke finger from mouth to earlobe	Head turns toward stimulus and mouth opens
Palmar/plantar grasp	Birth to 2–3 months	Stimulation of palm or plantar surface of foot	Palmar grasp/plantar flexion
Parachute	Appears at 9 months remains throughout life	Horizontal suspension and quick thrusting movement toward surface	Extension of extremities

WARD TIP

Developmental Evaluation
12 months: No babbling and no gesture
18 months: Less than 10 words
24 months: No two-word phrase, less that 30 words

EXAM TIP

At age 1 year, a child uses one word and follows a one-step command.

Development Delay

An 18-month-old infant brought in for temper tantrums has normal gross and fine motor skills but lacks language development and is cooperative and alert on exam. *Think: Hearing loss.*

Screening for hearing in the newborn nursery before discharge has resulted in earlier detection of hearing loss. Hearing impairment impacts language development. Inattention may be the initial presentation. It can also affect behavior and academic achievement.

DEFINITION

- Performance significantly below average in a given skill area.
- Prefer developmental delay: A condition in which a child is behind schedule in reaching milestones of early childhood development.
- Global developmental delay: Significant delay in two or more areas of development (gross or fine motor, speech and language, cognition, social and personal, and activities of daily living).
- Early detection of delay is important because brain development is most malleable in the early years of life.

ETIOLOGY

Most developmental disabilities are thought to be caused by a complex mix of factors. These factors include genetics; parental health and behaviors (such as smoking and drinking) during pregnancy; complications during birth; infections the mother might have during pregnancy or the baby might have very early in life; and exposure of the mother or child to high levels of environmental toxins.

- Cerebral palsy.
- Learning disabilities.
- Hearing and vision deficits.
- Autism.
- Neglect.
- Lack of exposure.
- Genetic diseases (Down syndrome, fragile X).
- Fetal alcohol syndrome.

DIAGNOSIS

- The Denver Development Assessment Test (Denver II) is a screening tool intended to be performed at well-child visits to identify children with developmental delay.
  - For children up to the age of 6 years.
  - Evaluates personal-social, fine motor, gross motor, and language skills.
- Clinical Adaptive Test (CAT)/Clinical Linguistic Auditory and Milestone Scale (CLAMS) rates problem solving, visual motor ability, and language development from birth to 36 months of age.
- Early intervention is important because the younger children are treated, the better the outcome.
- MCHAT (Modified Checklist for Autism in Toddlers): Autism screening tool administered at 18 months and 2 years.

Learning Disabilities (LDs)

- Present in 3–10% of children.
- To make a diagnosis of learning disability, the child must have a normal IQ.
- Include difficulties with reading (dyslexia), arithmetic (dyscalculia), and writing (dysgraphia).
  - Dyslexia is one of the most common learning disabilities.
  - Failure to acquire reading skills in the usual time course.
  - These children have excellent spoken language.
  - Presents with different degrees of severity.

Sleep Patterns

- Newborns sleep 18 hours per day, with 50% rapid eye movement (REM) sleep, compared to an adult with 20% REM sleep.
- By age 4 months, nighttime sleep becomes consolidated.
- Two sleep stages are REM (irregular pulse and time when dreaming occurs) and non-REM (deep sleep).
- Parasomnias (sleep disorders) begin near age 3 years.
- Nightmares occur during REM sleep—the child awakens in distress about a dream.

EXAM TIP

At age 2 years, a child uses two- to three-word phrases and follows two-step commands, and others can understand half of the child's language.

EXAM TIP

Lead exposure in children can lead to learning disabilities and attention-deficit disorder (ADD).

EXAM TIP

At age 3 years, a child uses three-word sentences, and others can understand three-fourths of the child's language.

EXAM TIP

At age 4 years, a child should be 40 lbs and 40 inches tall, and be able to draw a four-sided figure.

- Night terrors occur in non-REM sleep—the child appears awake and frightened but is not responsive, and then is amnestic about the event the next morning. Occurs between ages 2–8 years.
- Somnambulism (sleepwalking) occurs in non-REM sleep; most common in ages 4–8 years.
- Somniloquy (talking) is very common throughout life, sometimes accompanying night terrors and sleepwalking.

SLEEP RECOMMENDATIONS FOR CHILDREN

AGE	RECOMMENDED SLEEPING HOURS
Infants 4–11 months	12–15 hours
Toddlers 1–2 years	11–14 hours
Preschoolers 3–5 years	10–13 hours
School-aged children 6–13 years	9–11 hours

Nutrition

Newborn Nutrition

NEWBORN FEEDING TIPS

- For term newborns, caloric requirement is 100–120 kcal/kg/day (as compared to 1-year-old, 75 kcal/kg/day).
- Newborns grow at a rate of about 30 g/day.
- Newborns usually begin feeding within the first 6 hours of life.
- Newborns should be breast- or formula-fed every 3–4 hours thereafter.
- *Supply = demand*—the more often the baby breast-feeds, the more milk will be produced.
- After a period of 4–6 months of exclusive breast-feeding the mother should begin to introduce solid foods into the child's diet.
- If the child has stopped losing weight by 5–7 days and begins to gain weight by 12–14 days, then feeding is adequate.
- Hunger is not the only reason infants cry. They don't need to be fed every time they cry.
- Human milk is ideal for a term infant in first year of life.
- Whole cow's milk is not suitable for infants because the higher intake of sodium, potassium, and protein ↑ renal solute load.
- Cow's milk (whole milk until age 2) can be introduced after the first birthday.
- Optimal protein requirement of term infant is 2.2 g/kg body weight per day.

COLOSTRUM

- The first milk produced after birth.
- Usually a deep lemon color.
- Helps to clear bilirubin from the gut, produced from the high red blood cell turnover during blood volume contraction in the first weeks of life, which helps prevent jaundice.
- High in protein, minerals, immunologic factors, and antimicrobial peptides such as lactoferrin and lactoperoxidase; low in carbohydrates and fat.

BENEFITS OF BREAST-FEEDING

- Infant:
  - ↓ incidence of infection (i.e., otitis media, pneumonia, meningitis, bacteremia, diarrhea, urinary tract infection [UTI], botulism, necrotizing enterocolitis).
  - **Higher levels of immunologic factors**—immunoglobulins, complement, interferon, lactoferrin, lysozyme.
  - **↓ exposure to enteropathogens.**
  - Other postulated benefits include higher IQ, better vision, ↓ risk of sudden infant death syndrome (SIDS), less fussy eaters, may prevent obesity.
  - ↓ incidence of chronic disease (type 1 diabetes, lymphoma, Crohn disease/ulcerative colitis [UC], celiac disease, allergies).
- Maternal:
  - ↑ maternal oxytocin levels.
  - ↓ postpartum bleeding.
  - More rapid involution of uterus.
  - Less menstrual blood loss.
  - Delayed ovulation.

- Improved bone mineralization.
- ↓ risk of ovarian and breast cancer.
- Psychological benefits: ↑ maternal-child bonding.
- Other: Saves money for family and society, no risk of mixing errors, correct temperature, convenient, no preparation.

COMMON PROBLEMS WITH BREAST-FEEDING

- Soreness of nipples: Not due to prolonged feeding—due to improper positioning and poor removal.
- Engorgement: Unpleasant/painful swelling of the breasts when feeding cycle is ↓ suddenly (relieved by ↑ feeding on affected breast).
- Maternal fatigue, stress, and anxiety. Affects hormones needed for lactation.
- Fear of inadequate milk production, → formula milk supplementation.
- As the infant begins to feed less often, less milk is naturally produced. This often causes mother to misconceive that she is not producing enough milk to nourish the baby. Because of this, mother will frequently begin supplementing her milk with bottle milk, beginning a cycle of longer intervals between feeding, which causes less and less milk to actually be produced.
- Jaundice (see Table 5-1 and Gestation and Birth chapter).
- Possible vitamin deficiencies—A, D, K, B_{12}, thiamine, riboflavin.
- Infants who are exclusively breast-fed should receive vitamin drops after age 4 months.

CONTRAINDICATIONS TO BREAST-FEEDING

- Breast cancer.
- Cancer chemotherapy.
- Some medications (such as antimetabolites, chloramphenicol methimazole, tetracycline).
- Street drugs.
- Herpetic breast lesions.
- Untreated, active tuberculosis.
- Cytomegalovirus (CMV) infection.
- Human immunodeficiency virus (HIV) infection.
- In developing countries where food is scarce and HIV is endemic, the World Health Organization recommends breast-feeding by HIV-infected moms because the benefits outweigh the risks.

EXAM TIP

Cow's milk predominant protein is casein (78%).

WARD TIP

Breast-fed infant requires the following supplements:
- Vitamin K 1 mg IM at birth
- Vitamin D 400 IU/day
- Fluoride (after 6 months)
- Iron from 4 to 12 months

WARD TIP

Tell the breast-feeding mother: If the baby doesn't let go, break the suction by inserting finger into corner of mouth; don't pull.

EXAM TIP

Breast-feeding jaundice occurs in the first week. Breast milk jaundice starts at 1 week of life, up to 3 weeks of age.

WARD TIP

Oral contraceptive is not a contraindication for breast-feeding.

TABLE 5-1. **Breast-Feeding versus Breast Milk Jaundice**

BREAST-FEEDING JAUNDICE	BREAST MILK JAUNDICE
Also called "not enough milk jaundice"—usually due to ↓ or poor milk intake.	Syndrome of prolonged unconjugated hyperbilirubinemia that is thought to be due to an inhibitor to bilirubin conjugation in the breast milk of some mothers.
Occurs *during* first week of life.	Begins *after* first week of life; peaks usually after second to third week.
Reduced enteral intake, → infrequent and scanty bowel movements and ↑ enterohepatic circulation of bilirubin.	Transient unless severe unconjugated hyperbilirubinemia.
	No treatment necessary.

- Galactosemia: Infants with galactosemia should not ingest lactose-containing milk.
- Maternal hepatitis A, B, and C are usually not transmitted through breast-feeding. The infant must be immunized against hepatitis B.

SIGNS OF INSUFFICIENT FEEDING OF INFANT

- Fewer than six wet diapers per day after age 1 week (before that, count one wet diaper per age in days for first week of life).
- Continual hunger, crying.
- Continually sleepy, lethargic baby.
- Fewer than seven feeds per day.
- Long intervals between feedings.
- Sleeping through the night without feeding.
- Loss of >10% of weight.
- ↑ jaundice.

REASONS FOR FAILURE TO GROW AND GAIN WEIGHT

An 18-month-old African immigrant male is brought in by his parents for a health evaluation. The family members are refugees. As you examine the child, you find that he is in the bottom 2% in both height and weight and is thin looking. The parents deny any childhood illnesses and state that the child has never been severely ill. Blood tests including complete blood count, chemistry, and liver function tests are within normal limits, and albumin is 2.3. What is the diagnosis? Failure to thrive (FTT). It is a condition when physical growth of a child is below the third or fifth percentile. Nonorganic or psychosocial FTT is more common. The laboratory evaluation is usually normal and should be obtained judiciously. Obtaining a detailed history is the most important part of evaluation, which helps to determine whether the cause is organic or nonorganic.

- Improper formula preparation.
- Use of skim and 2% milk before age 2.
- Prolonged use of diluted formula.
- Prolonged use of BRAT (bananas, rice, applesauce, toast) diet after illness.
- Excessive juice or water.
- Inappropriate feeding schedule.

FORMULA

- Types (see Table 5-2).
- Inappropriate formulas (see Table 5-3).
- Hydrolysate formula:
    - Formula with peptides: Nutramigen, Pregestimil, Alimentum.
    - Formulas with free amino acids: Neocate, Elecare.

SOLID FOODS

- Solid food should be introduced between 4 and 6 months; introducing solids before this time does not contribute to a healthier child, nor does it help the infant to sleep better.
- New foods should be introduced individually and about a week apart; this is done to identify any allergies and intolerance the child may have

T A B L E 5 - 2 .   **Formulas**

FORMULA	INDICATIONS	FORMULATIONS
Cow's milk based (Examples: Enfamil, Similac)	Premature	Lactose-free
	Transitional	Low electrolyte
		Low iron
		Whey hydrosylate
Soy protein based (Examples: Isomil, Prosobee)	Galactosemia	Carbohydrate free
	Lactose intolerance	Fiber-containing
		Sucrose free Lower whey-to-casein ratio
Protein hydrosylate	Malabsorption	
	Food allergies	
Amino acid based	Food allergies	
	Short gut	
High medium-chain triglyceride oil	Chylous ascites Chylothorax	
Metabolic		Lofenelac
		Phenex-1—phenylketonuria (PKU)
		Propimex-1—propionic acidemia

T A B L E 5 - 3 .   **Inappropriate Formulas**

Cow's milk	↓ iron, essential fatty acids, vitamin E
	↑ sodium, potassium, chloride, and protein
Goat's milk	Allergen potential
	Very high potential renal solute load High protein
	Low in folate and iron
	Questionable pasteurization
Rice milk	Very low in protein and fat
	Low in electrolytes and almost all vitamins and minerals
Commercial soy milk (not soy formula)	Soy induces L-thyroxine depletion through fecal waste, creating an ↑ requirement for iodine, potentially → goiter

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EXAM TIP

Predominant fat in preterm infant formula is medium-chain triglycerides.

WARD TIP

Formula for an infant who is allergic to both cow milk and soy protein: hydrolysate formula.

WARD TIP

Do not give an infant under 6 months of age water or juice (water fills them up; juice contains empty calories, and excess sugar can cause diarrhea).

T A B L E 5 - 4 .   Daily Caloric Requirements

AGE	MALES (KCAL)	FEMALES (KCAL)
0–3 months	545	515
4–6 months	690	645
7–9 months	825	765
10–12 months	920	865
1–3 years	1230	1165
4–6 years	1715	1545
7–10 years	1970	1740
11–14 years	2220	1845
15–18 years	2755	2110

(rash, vomiting, diarrhea). There are many suggested orders in which to introduce new food. A common one is vegetable first, green to orange, and then fruits, to introduce foods from most bland to sweetest.

READINESS FOR SOLID FOODS

- Hand-to-mouth coordination.
- ↓ tongue protrusion reflex.
- Sits with support.
- Lack of head lag.
- Drooling.
- Opens mouth to spoon.

CALORIC REQUIREMENTS

Estimated average requirement: Basal metabolic rate × physical activity level (see Table 5-4).

Fluid Management

PHYSIOLOGIC COMPARTMENTS

Total Body Water (TBW)

TBW makes up 50–75% of the total body mass depending on age, sex, and fat content.

Distribution
- Intracellular fluid accounts for two-thirds of TBW and 50% of total body mass.
- Extracellular fluid accounts for one-third of TBW and 25% of total body mass.

WARD TIP

Do not use 2% milk before 2 years of age or skim milk before 5 years.

WARD TIP

Typical formulas contain 20 kcal/ounce.

WARD TIP

Avoid foods that are choking risks, including small fruits, raw vegetables, nuts, candy, and gum.

WARD TIP

Neonates have a greater percentage of TBW per weight than do adults (about 70–75%).

TABLE 5-5. **Signs and Symptoms of Dehydration**

	MILD	MODERATE	SEVERE
% Body weight loss	3–5%	6–9%	> 10%
General	Consolable	Irritable	Lethargic/obtunded
Heart rate	Regular	↑	More ↑
Blood pressure	Normal	Normal/low	Low
Tears	Normal	Reduced	None
Urine	Normal	Reduced	Oliguric/anuric
Skin turgor	Normal	Tenting	None
Anterior fontanel	Flat	Soft	Sunken
Capillary refill	< 2 sec	2–3 sec	> 3 sec
Mucous membranes	Moist	Dry	Parched/cracked

Extracellular Fluid (ECF)

ECF is composed of plasma (intravascular volume) and interstitial fluid (ISF).

Dehydration

- Definition: Body fluid depletion (see Table 5-5).
- Causes can be divided into two categories:
    - ↓ intake.
    - ↑ loss (e.g., vomiting, diarrhea).
- → hypovolemia, gradually affecting each organ system.

FLUID THERAPY

Goals

Rapidly expand the ECF volume and restore tissue perfusion, replenish fluid and electrolyte deficits, meet the patient's nutritional needs, and replace ongoing losses.

Methods

- Fluid requirements can be determined from caloric expenditure.
- For each 100 kcal metabolized in 24 hours, the average patient will require 100 mL of water, 2–4 mEq Na^+, and 2–3 mEq K^+.
- This method overestimates fluid requirements in neonates under 3 kg.
- For a child over 20 kg, give 1500 mL + 20 mL/kg for each kilogram over 20 kg.

Maintenance

- Replacement of *normal* body fluid loss.
- Causes of normal fluid loss include:
    - Insensible fluid loss (i.e., lungs and skin).
    - Urinary loss.

WARD TIP

You know a patient is dehydrated when he or she is **PARCHED**:

Pee, **P**ressure (blood)
Anterior fontanel
Refill, capillary
Crying
Heart rate
Elasticity of skin
Dryness of mucous membranes

WARD TIP

Percentage of dehydration can be estimated using (pre-illness weight – illness weight / pre-illness weight) × 100%.

WARD TIP

For convenience, use the Holliday-Segar method to determine maintenance intravenous (IVF) requirements:

- Give 100 mL/kg of water for the first 10 kg.
- For a child over 10 kg but under 20 kg, give 1000 mL + 50 mL/kg for each kilogram over 10 kg.

1 kg = 2.2 lbs

TABLE 5-6.   Calculating Maintenance Fluids per Day

BODY WEIGHT (KG)	MILLILITERS PER DAY	MILLILITERS PER HOUR
0–10	100/kg	4/kg
11–20	1000 + 50/kg over 10	40 + 2/kg over 10
>20	1500 + 20/kg over 20	60 + 1/kg over 20

- Water requirements (mL/100 calories metabolized/day): Insensible—skin, 30; lungs, 15; stool, 5; urine, 50.

Deficit

- Replacement of *abnormal* fluid and electrolyte loss (i.e., from vomiting, diarrhea, etc).
- Example: For a 25-kg patient, 100 (for first 10 kg) × 10 + 50 (for second 10 kg) × 10 + 20 (for remainder) × 10 = 1600 mL/day or 65 mL/hr when divided by 24 hours.

DEFICIT THERAPY

Hyponatremia

In hypotonic (hyponatremic) dehydration, serum $Na^+ < 130$ mEq/L.

EPIDEMIOLOGY

- Most common electrolyte abnormality.
- More common in infants fed on tap water.

ETIOLOGY

- Hypervolemic hyponatremia—fluid retention:
  - Congestive heart failure (CHF).
  - Cirrhosis.
  - Nephrotic syndrome.
  - Acute or chronic renal failure.
  - Capillary leak due to sepsis.
  - Hypoalbuminemia due to gastrointestinal disease.
- Hypovolemic hyponatremia—↑ sodium loss:
  - Due to renal loss:
    - Diuretic excess, osmotic diuresis, salt-wasting diuresis.
    - Adrenal insufficiency, pseudohypoaldosteronism.
    - Proximal renal tubular acidosis.
    - Metabolic alkalosis.
  - Due to extra-renal loss:
    - Gastrointestinal (GI)—vomiting, diarrhea, tubes, fistula.
    - Sweat.
    - Third-spacing—pancreatitis, burns, muscle trauma, peritonitis, effusions, ascites.
- Euvolemic hyponatremia:
  - Syndrome of inappropriate antidiuretic hormone secretion (SIADH):
    - Hospitalized children are at ↑ risk for nonphysiologic secretion of ADH.

WARD TIP

Calculations for fluid therapy are just estimates—you must monitor the success of fluid replacement by measuring ins and outs, body weight, and clinical picture (see Table 5-6).

WARD TIP

4-2-1 IVF RULE: To determine rate in milliliters per hour, use 4 (for first 10 kg) × 10 kg + 2 (for second 10 kg) × 10 kg + 1 (for remainder) × remaining kg = 65 mL/hr.

WARD TIP

Hyponatremia can be factitious in the presence of high plasma lipids or proteins; consider the presence of another osmotically active solute in the ECF such as glucose or mannitol when hypotonicity is absent.

EXAM TIP

SIADH:
- Euvolemia
- Low urine output
- High urinary sodium loss
- Treat with fluid restriction

- Tumors.
- Chest disorders.
- Central nervous system (CNS) disorders—infection, trauma, shunt failure.
- Drugs—vincristine, vinblastine, diuretics, carbamazepine, amitriptyline, morphine, isoproterenol, nicotine, adenine arabinoside, colchicine, barbiturates.
  - Glucocorticoid deficiency.
  - Hypothyroidism.
  - Water intoxication due to intravenous (IV) therapy, tap water enema, or psychogenic (excess water drinking).
  - Polydipsia.

SIGNS AND SYMPTOMS

- Symptoms may occur at serum concentrations of ≤125 mEq/L.
- Cerebral edema—more pronounced in acute.
- Early: Anorexia, nausea, headache.
- Mental status changes.
- Later: Beware of brain herniation—posturing, autonomic dysfunction, respiratory depression, seizures, and coma.
- Central pontine myelinolysis can occur if hyponatremia is corrected too quickly.

DIAGNOSIS

- Volume status.
- Acute versus chronic.
- Serum and urine osmolality and sodium concentration, blood urea nitrogen (BUN), creatinine, other labs (glucose, aldosterone, thyroid-stimulating hormone [TSH], etc).

TREATMENT

- Na^+ deficit: (Na^+ desired – Na^+ observed) × body weight (kg) × 0.6.
- One half of the deficit is given in the first 8 hours of therapy, and the rest is given over the next 16 hours.
- Deficit and maintenance fluids are given together.
- If serum Na^+ is <120 mEq/L and CNS symptoms are present, a 3% NaCl solution may be given IV over 1 hour to raise the serum Na^+ over 120 mEq/L.

Hypernatremia

In hypertonic (hypernatremic) dehydration, serum Na^+ > 150 mEq/L.

ETIOLOGY

- ↓ water or ↑ sodium intake.
- ↓ sodium or ↑ water output.
- Diabetes insipidus (either nephrogenic or central) can cause hypernatremic dehydration secondary to urinary free water losses.
- Hypovolemic hypernatremia:
  - Extrarenal or renal fluid losses.
  - Adipsic hypernatremia is secondary to ↓ thirst—behavioral or damage to the hypothalamic thirst centers.
- Hypervolemic hypernatremia:
  - Hypertonic saline infusion.
  - Sodium bicarbonate administration.
  - Accidental salt ingestion.
  - Mineralocorticoid excess (Cushing syndrome).

WARD TIP

The rise in serum Na^+ in the correction of chronic hyponatremia should not exceed 2 mEq/L/hr or cerebral pontine myelinosis may occur secondary to fluid shifts from the intracellular fluid.

WARD TIP

The fluid deficit plus maintenance calculations generally approximate 5% dextrose with 0.45% saline; 6 mL/kg of 3% NaCl will raise the serum Na^+ by 5 mEq/L.

WARD TIP

Look for a low urine specific gravity (<1.010) in diabetes insipidus. These patients appear euvolemic because most of the free water loss is from intracellular and interstitial spaces, not intravascular.

- Euvolemic hypernatremia:
    - Extrarenal losses—↑ insensible loss.
    - Renal free water losses—central diabetes insipidus (DI), nephrogenic DI.

SIGNS AND SYMPTOMS

- Anorexia, nausea, irritability.
- Mental status changes.
- Muscle twitching, ataxia.

TREATMENT

- The treatment of elevated serum Na^+ must be done gradually at a rate of ↓ around 10–15 mEq/L/day.
- Usually, a 5% dextrose with 0.2% saline solution is used to replace the calculated fluid deficit over 48 hours after initial restoration of adequate tissue perfusion using isotonic solution.
- If the serum Na^+ deficit is not correcting, the free water deficit may be given as 4 mL/kg of free water for each milliequivalent of serum Na^+ over 145, given as 5% dextrose water over 48 hours.
- Too rapid correction of hypernatremia can result in cerebral edema.

Hypokalemia

Can be considered at $K^+ < 3.5$ mEq/L, but is extreme when $K^+ < 2.5$ mEq/L.

ETIOLOGY

Excess renin, excess mineralocorticoid, Cushing syndrome, renal tubular acidosis (RTA), Fanconi syndrome, Bartter syndrome, villous adenoma of the colon, diuretic use/abuse, GI losses, skin losses, diabetic ketoacidosis (DKA), transcellular shifts (alkalemia, insulin, refeeding syndrome), anorexia, insulin.

SIGNS AND SYMPTOMS

↓ peristalsis or ileus, hyporeflexia, paralysis, rhabdomyolysis, muscle cramps and weakness, and arrhythmias including premature ventricular contractions (PVCs), atrial nodal or ventricular tachycardia, and ventricular fibrillation.

DIAGNOSIS

- Serum value.
- Electrocardiogram (ECG) may demonstrate flattened T waves, shortened PR interval, and U waves.

TREATMENT

- Consider cardiac monitor.
- **If potassium is dangerously low (<2.5 mEq/L) and patient is symptomatic, IV potassium must be given.**
- Do not exceed the rate of 0.5 mEq/kg/hr.
- Oral potassium may be given to replenish stores over a longer period of time. Common forms of potassium include the chloride, phosphate, citrate, and gluconate salts.

Hyperkalemia

- Mild to moderate: $K^+ = 6.0–7.0$.
- Severe: $K^+ > 7.0$.

ETIOLOGY

Renal failure, hypoaldosteronism, aldosterone insensitivity, K$^+$-sparing diuretics, cell breakdown, metabolic acidosis, transfusion with aged blood, hemolysis, leukocytosis, rhabdomyolysis, tumor lysis syndrome, exercise, malignant hyperthermia, lupus nephritis, NSAIDs, heparin.

SIGNS AND SYMPTOMS

Muscle weakness, paresthesias, tetany, ascending paralysis, and arrhythmias including sinus bradycardia, sinus arrest, atrioventricular block, nodal or idioventricular rhythms, and ventricular tachycardia and fibrillation.

DIAGNOSIS

- Serum value.
- ECG may demonstrate peaked T waves and wide QRS.

TREATMENT

- If hyperkalemia is severe or symptomatic, first priority is to stabilize the cardiac membrane. Administer calcium chloride or gluconate (10%) solution under close cardiac monitoring.
- Sodium bicarbonate, albuterol nebulizer, or glucose plus insulin can be given to shift K$^+$ to the intracellular compartment.
- Kayexalate resin can be given to bind K$^+$ in the gut (works the slowest).
- Furosemide can be given to enhance urinary K$^+$ excretion.
- In extreme cases, hemo- or peritoneal dialysis may be necessary.

Vitamin and Mineral Supplements

FLUORIDE

- Supplement after age 6 months if the water is not fluorinated sufficiently (particularly well water).
- If <0.3 ppm, supplement with 0.25 mg/day for children 6 months to 3 years.
- Deficiency: Dental caries.
- Excess: Fluorosis—mottling, staining, or hypoplasia of the enamel.
- Children under 6 years should be supervised when brushing to avoid risk of swallowing toothpaste. Children <2 years of age should use a "smear" of fluoridated toothpaste, and children <6 years of age should use a small pea-sized amount.

> **WARD TIP**
>
> Because of the ↑ risk for fluorosis, don't give fluoride supplements before age 6 months!

VITAMIN D

- Vitamin D is critical for skeletal development and cellular function because of its effect on calcium homeostasis (by promoting intestinal calcium absorption).
- Breast milk typically contains about 25 IU/L of vitamin D, which is insufficient for rickets prevention.
- Deficiency can occur if exclusively breast-fed, breast-feeding infant's mother has insufficient intake, or the infant is fed on whole cow's milk.
- Supplementation is with 400 IU/day.
- Deficiency: Impaired mineralization of bone tissue (osteomalacia) and of growth plates (rickets).
- Vitamin D deficiency can → hypocalcemia.

> **WARD TIP**
>
> Most bottled water is not fluorinated.

IRON

A 4-year-old female was brought in by EMS with a complaint from the mother that the child had a sudden onset of diarrhea and vomiting. The mother reports blood in the vomitus. On examination, the child is very irritable. She is breathing very rapidly, and her heart rate is 167 beats/min, with a blood pressure of 96/57 mm Hg. The mother states that she is a healthy child with no recent illnesses and is up to date on all her vaccinations. There has been no recent travel, and the child's 3-year-old brother is not ill. There has been no change in the child's diet. The mother states that she is very conscientious of the diets in the house, as she is trying to get pregnant again and is taking prenatal vitamins. What is the diagnosis? Iron overdose.

Iron poisoning is one of the most fatal in children. Iron preparations are readily available due to their widely prescribed use in prenatal care. It is particularly attractive to young children because these brightly colored tablets appear similar to candy. In addition, often some iron preparations are coated with sucrose to make them palatable. Iron poisoning should be considered in a child with acute onset of vomiting and hypoperfusion. Serum iron levels should be obtained and are helpful in predicting the clinical course of the patient.

- Newborn iron stores are sufficient for 6 months in a term infant.
- Therefore, breast-fed infants need iron supplementation 1 mg/kg/day (i.e., iron-fortified cereals and baby foods), beginning at 4 to 6 months.
- Preterm breast-fed infants should receive 2 mg/kg/day starting at 2 months of age.
- Deficiency: Anemia (hypochromic microcytic) and growth failure.
- Only iron-fortified formula should be used for weaning or for supplementing breast milk in children younger than 12 months.

VITAMIN K

- Human breast milk is deficient in vitamin K.
- Infant has a limited body store of vitamin K.
- Therefore, it is necessary to administer a 1-mg vitamin K IM injection at birth. Recommended for every newborn, not just breast-fed.
- Deficiency: Thought to contribute to hemorrhagic disease of the newborn.
- Vitamin K is necessary for the synthesis of clotting factors II, VII, IX, and X.
- Fat soluble: Requires bile salts for absorption.

ZINC

- Deficiency-associated intestinal malabsorption, nutritional intake limited to breast milk.
- Deficiency used to be associated with total parenteral nutrition (TPN); now formulas have zinc in them.
- Deficiency manifests as acrodermatitis, alopecia, and growth failure.

VITAMIN A

A 14-month-old infant presents with anorexia, pruritus, and failure to gain weight; he has a bulging anterior fontanel and tender swelling over both tibias. The mother buys all food at a natural foods store. *Think: Hypervitaminosis A.*

Central nervous system, liver, bone, and skin and mucous membranes are the common sites. Acute vitamin A toxicity is not common. Initial presentation is primarily neurologic. Symptoms include irritability, tiredness, and somnolence. A bulging fontanel due to increased intracranial pressure may be present in infants. Pain and tenderness, particularly in the long bones, is often present.

- Hypervitaminosis A.
- Congenital absence of enzymes needed to convert provitamin A carotenoids to vitamin A.
- Acute:
  - Pseudotumor cerebri: Bulging fontanel, drowsiness, cranial nerve palsies.
  - Nausea, vomiting.
- Chronic:
  - Poor weight gain.
  - Irritability.
  - Tender swelling of bones—hyperostosis of long bones, craniotabes; ↓ mineralization of skull.
  - Pruritus, fissures, desquamation.

OTHER SUPPLEMENTS

- If mother is a strict vegetarian, supplement thiamine and vitamin B_{12}.
- Thiamine deficiency causes beriberi (weakness, irritability, nausea, vomiting, pruritus, tremor, possible congestive heart failure).
- Human milk will have adequate vitamin C only if mother's intake is sufficient.
- Commercial formula is often modified from cow's milk and fortified with vitamins and minerals so that no additional supplements are needed for the full-term infant.

Obesity

> A 16-year-old female presents to her primary care physician for a routine health visit. Upon questioning she states that she is very concerned about becoming overweight and that she goes to the gym often but wants nutritional advice. On examination, she is very thin and emaciated with very little subcutaneous fat, and you notice a thin layer of hair on her arms. She states that she is not sexually active and her last menstrual period was 4 months ago. What is the diagnosis? Anorexia nervosa.

DEFINITION

- Overweight is defined as a body mass index (BMI)-for-age 85–94th percentile, obese is 95–98th percentile, and severely obese is >99th percentile on the Centers for Disease Control and Prevention (CDC) growth charts.
- BMI is calculated by dividing weight (in kilograms) by height (in meters squared).
- Adults:
  - Normal BMI: 18.5–24.9 kg/m^2.
  - Overweight: 25.0–29.9 kg/m^2.
  - Obesity: 30.0–39.9 kg/m^2.
  - Extreme obesity: >40 kg/m^2.
  - Obesity: BMI of ≥30.

RISK FACTORS

- Excessive intake of high-energy foods ("empty" calories).
- Inadequate exercise in relation to age and activity, sedentary lifestyle.
- Low metabolic rate relative to body composition and mass.

EXAM TIP

Vitamin A deficiency is the number 1 worldwide most common cause of blindness in young children.

- Genetics: Strong relationship between BMI of children and their biologic parents:
    - If one parent is obese, risk of obesity as an adult is 40%.
    - If two parents are obese, risk of obesity as an adult is 80%.
- Certain genetic disorders (Alström syndrome, Carpenter syndrome, Cushing syndrome, Fröhlich syndrome, hyperinsulinism, Laurence-Moon-Bardet-Biedl syndrome, muscular dystrophy, myelodysplasia, Prader-Willi syndrome, pseudohypoparathyroidism, Turner syndrome).

COMPLICATIONS

- Negative social attitudes: Embarrassment, harassment, low self-esteem.
- Behavioral: Depression, anxiety, disordered eating, worsening school performance, social isolation.
- Respiratory: Obstructive sleep apnea, snoring.
- Orthopedic: Slipped capital femoral epiphysis (SCFE), back pain, joint pain.
- Endocrine: Type 2 diabetes mellitus, metabolic syndrome, PCOS.
- Cardiovascular: Hypertension, hyperlipidemia.
- Gastrointestinal: Gallbladder disease, nonalcoholic fatty liver disease.

PREVENTION

- Early awareness and starting good eating and exercise habits early may hinder the development of overeating and obesity.
- Parent education is paramount in providing guidance in appropriate nutrition and feeding habits to promote healthy lifestyles for children.
- Certain cultures are more predisposed to overfeed children when children are upset.
- Newborns need all the nourishment they can get. They need to be fed on a continuous schedule and on demand.
- Within the first year, offer food only when the child is hungry.
- Have predictable eating schedules and offer child-sized portions using child-sized plates.
- Avoid using food as reward or punishment.

DIAGNOSIS

BMI is the most useful index for screening for obesity. It correlates well with subcutaneous fat, total body fat, blood pressure, blood lipid levels, and lipoprotein concentrations in adolescents.

TREATMENT

- Adherence to well-organized program that involves both a balanced diet and exercise.
- Behavioral modification.
- Involvement of family in therapy.
- Surgery and pharmacotherapy are relatively contraindicated in children.
- Very-low-calorie diets are detrimental to growth and development—all nutritional needs should be met.
- Avoid rapid ↓ in weight.
- Goal of effective weight reduction is not so much to lose pounds but to maintain weight through growth spurt.
- If BMI is >97th percentile for age and sex, weight reduction may be recommended even prior to pubertal growth spurt.

WARD TIP

There is a direct relationship between degree of obesity and severity of medical complications.

WARD TIP

Obesity makes SHADE:
  SCFE
  Hypertension
  Apnea (sleep)
  Diabetes
  Embarrassment

Health Supervision and Prevention of Illness and Injury in Children and Adolescents

Morbidity and Mortality

- The leading cause of death in children **under 1 year of age** is grouped under the term *perinatal conditions*, which include:
  - Congenital malformation, deformations, and chromosomal abnormalities (number one cause).
  - Low birth weight.
  - Sudden infant death syndrome (SIDS).
  - Respiratory distress syndrome.
  - Complications of pregnancy.
  - Perinatal infections.
  - Intrauterine or birth hypoxia.
- From **1 year to 24 years of age,** the leading cause of death is injury (unintentional injuries).

Prevention

Prevention is of primary importance in caring for the pediatric patient and is promoted through:

- Parental guidance (anticipatory guidance and counseling).
- Screening tests.
- Immunization.

Parental Guidance

Age-appropriate anticipatory guidance is provided to parents at various well-child visits.

1 WEEK–1 MONTH

A 1-month-old infant is brought to the ED with poor feeding, weak suck, drooling, constipation, and ↓ spontaneous movements. He is exclusively breast-fed, and his mother has been giving him a home remedy for "colic." Physical exam is positive for hypotonia. *Think: Botulism* and its relationship with some home remedies prepared with honey. Treatment is with human botulism immune globulin (BIG-IV).

- Place infant to sleep on back to prevent sudden infant death syndrome (SIDS). Never on the stomach or side.
- Keep soft objects and loose bedding such as comforters, pillows, bumper pass, and stuffed animals in crib with infant.
- Use a car seat. Rear facing in back seat.
- Know signs of an illness.
- Use a rectal thermometer.
- Maintain a smoke-free environment.
- Maintain water temperature at <120°F (48.8°C). Takes 10 minutes to get a burn at this temperature if baby is exposed.
- Do not give honey to a child under 1 year of age (risk for botulism).
- Discuss normal crying behavior and give some suggestions for how to calm the infant.

- Techniques to calm infant: swaddling in a light blanket, rocking in a cradle, windup swing, vibrating chair.
- Never shake your baby.
- Assess parental well-being. Baby blues are normal but if they persist beyond 2 weeks provide resources for mother's postpartum depression.

2 MONTHS–1 YEAR

- Childproof home to keep children safe from poisons, household cleaners, medications, buckets and tubs filled with water, plastic bags, electrical outlet covers, hot liquids, matches, small and sharp objects, guns, and knives.
- The American Academy of Pediatrics (AAP) does not recommend syrup of ipecac anymore. Give telephone number to local poison control hotline.
- No solid food until 4–6 months.
- Introduce single ingredient foods one at a time to assess for allergies.
- Limit juice to less than 4 ounces a day.
- Avoid baby walkers.
- Do not put baby to bed with bottle, as it can cause dental caries.
- Breast-feed or give iron-fortified formula, but no whole milk until after 1 year of age.
- Avoid choking hazards such as coins, peanuts, popcorn, carrot sticks, hard candy, whole grapes, and hot dogs.
- May start using sippy cup at 6–9 months.
- Do not leave baby alone in tub or high places.
- Do not drink hot liquids while holding your baby.
- Importance of tummy time to meet milestones and decrease positional plagiocephaly.
- Visit the dentist by 12 months or after first tooth erupts.

1–5 YEARS

- Use toddler car seat (ages 1–4) and booster seat (ages 4–8) if proper weight and height. See car seat section.
- Brush teeth, see dentist. Brush teeth twice daily with plain water and a soft toothbrush
- Wean from bottle (start by 9 months of age with the introduction of cup).
- Make sure home is childproof again.
- Restrict child's access to stairs.
- Allow child to eat with hands or utensils.
- Use sunscreen (can use as early as 6 months).
- Wear properly fitting bicycle helmet.
- Provide close supervision, especially near dogs, driveways, streets, and lawnmowers.
- Make appointment with dentist by 1 year of age.
- Ensure that child is supervised when near water; build fence around swimming pool with latched gate.
- Screen for amblyopia, strabismus, and visual acuity in all children younger than 5 years.
  - Strabismus: Cover test or Hirschberg light reflex test in children <3 years.
  - Visual acuity: >3 years and screen every 1–2 years throughout childhood.

6–10 YEARS

- Reinforce personal hygiene.
- Teach stranger safety.

EXAM TIP

Any child with a rectal temperature >100.4°F (38°C) in the first 2 months of life should be seen immediately, to rule out sepsis with GBS, *Listeria, E. Coli.*

WARD TIP

Assess head control before allowing baby to start solid foods to decrease the risk of choking.

EXAM TIP

Falls and drowning are major risks of injury and death in toddlers.

EXAM TIP

Most infants drown in their own bathtub.

WARD TIP

- Early childhood caries (cavities) is the number 1 chronic disease affecting young children.
- Early childhood caries is five times more common than asthma and seven times more common than hay fever.

WARD TIP

Temperature of the water heater should be kept below 120°F (49°C) to prevent accidental scalding injuries.

- Provide healthy meals and snacks. Eat 5+ servings of fruits and vegetables a day; eat breakfast.
- Limit screen time to less than 2 hours a day.
- Be physically active 60 minutes a day.
- Keep matches and guns out of children's reach.
- Use seat belt always, and booster seat until 4 feet 9 inches in height.
- Brush teeth twice daily with pea-sized amount of fluoride toothpaste.
- Limit screen time to less than 2 hours a day.
- Visit dentist 2×/year.
- Teach pedestrian safety.
- Teach child to swim.

11–21 YEARS

- Continue to support a healthy diet and exercise.
- Wear appropriate protective sports gear.
- Counsel on safe sex and avoiding alcohol and drugs.
- Promote a healthy social life, balanced diet, and at least 60 minutes of exercise every day, with 30 minutes of vigorous exercise 3×/week.
- Ask about mood or eating disorders (see below).
- Address school performance, homework, and bullying.

Screening

BLOOD PRESSURE

- High blood pressure (hypertension) in children is blood pressure that's the same as or higher than 95% of children who are the same sex, age, and height as your child.
- Routine monitoring of blood pressure should begin at age 3 years.
- Most common cause of high blood pressure reading in children is inappropriate cuff size.
- High blood pressure can be primary or secondary, the younger the child and the higher the blood pressure, the greater the high blood pressure has an identifiable cause.
- Other causes of high blood pressure in children: heart and kidney diseases; medications; endocrine disorders.
- Contributing factors: Family history, race, excess weight, or obesity.

METABOLIC SCREENING

At 24 hours of life, the neonate should receive screening for various metabolic disorders including hypothyroidism, phenylketonuria (PKU), sickle cell disease, and adrenal cortex abnormalities.

Newborn screens test for diseases that if caught early are manageable and will prevent long-term poor health outcomes

LEAD SCREENING

- Exposure is ↑ by:
  - Living in or visiting a house built before 1978 with peeling or chipped paint.
  - Plumbing with lead pipes or lead solder joints.

Common Causes of Hypertension by Age

INFANTS	CHILDREN		ADOLESCENTS
	1-6 Y	7-12 Y	
Thrombosis of renal artery or vein	Renal artery stenosis	Renal parenchymal disease	Essential hypertension
Congenital renal anomalies	Renal parenchymal disease	Renovascular abnormalities	Renal parenchymal disease
Coarctation of aorta	Wilms tumor	Endocrine causes	Endocrine causes
Bronchopulmonary dysplasia	Neuroblastoma	Essential hypertension	
	Coarctation of aorta		

- Living near a major highway where soil may be contaminated with lead.
- Contact with someone who works with lead.
- Living near an industrial site that may release lead into the environment.
- Taking home remedies that may contain lead.
- Toys from abroad.
- Traditional cosmetics: Kohl is a traditional cosmetic, often used as eyeliner.
- Having friends/relatives who have had lead poisoning.
- Screen for lead levels at age 12 months and 24 months.

HEMATOCRIT

- Screen for anemia at 9–12 months of age where certification is needed for WIC (Women, Infants, and Children) or if the appropriate risk factors are present.
- Second test 6 months later in high-risk communities for iron deficiency.
- Anemia: Hemoglobin levels <11 g/dL.
- Risk factors for anemia include low socioeconomic status, birth weight under 1500 g, whole milk received before 6 months of age, low-iron formula given, low intake of iron-rich foods.

HYPERLIPIDEMIA

- Screen for hyperlipidemia in children older than 2 years with appropriate risk factors:
  - Family history of coronary or peripheral vascular disease before the age of 55 years in parents or grandparents.
  - Parent with a total serum cholesterol level >240 mg/dL.
  - Obesity.
  - Hypertension.
  - Diabetes mellitus.
- Screening may also be considered in children with inactivity; also in adolescents who smoke.
- All children should be screened between 9 and 11 years and again between 17 and 21 years.

WARD TIP

Infants and young children are more likely to be exposed to lead than are older children. They may chew paint chips, and their hands may be contaminated with lead dust. Young children also absorb lead more easily and sustain more harm from it than do adults and older children.

EXAM TIP

Children's blood lead levels increase most rapidly at 6–12 months and peaks at 18–24 months.

VISION AND HEARING

- A hearing screen is recommended shortly after birth, ideally before discharge from the newborn nursery.
- Vision screening may begin at age 3 years, sooner if concerns.
- Suspect hearing loss earlier if child's speech is not developing appropriately.
- A child's cooperation is essential to obtaining an accurate result (~3 years).

AAP Car-Seat Recommendations

Infants and toddlers: Rear facing only or rear facing convertible (until 2 years and 20 lbs).
Toddlers and preschoolers: Convertible or forward facing with harness (until 4 years and 40 lbs).
School aged: Booster seats (until 4 feet 9 inches tall).
Older children: When large enough, use standard lap and shoulder belts. Younger than 13 should sit in backseat.
Other Car-Seat Note: Never place a car seat in front of an air bag (front passenger-side and side-impact air bags). The safest place for the infant is the middle portion of the rear seat.

Vaccines

- See latest CDC vaccine schedule (Figure 6-1).
- Site of injection:
    - Infants: Anterolateral thigh.
    - Children: Deltoid.

HEPATITIS B

A 25-year-old female who is hepatitis B surface antigen positive is about to deliver a baby and she asks what is the best way to prevent the baby from having hepatitis B. *Think: Prevention.*

Babies born to women who are hepatitis B surface antigen positive receive hepatitis B immunoglobulin and hepatitis B vaccine shortly after birth, and 1–2 months after completing three doses of hepatitis B vaccine, they should be tested for hepatitis B surface antigen as well as the antibody.

- First dose given intramuscularly (IM) at birth or within first 2 months of life.
- Second dose given 1 month after first dose.
- Third dose given 4 months after first dose and 2 months after second dose, but not before 6 months of age.
- Must give at birth along with hepatitis B immune globulin (HBIG) if baby is exposed transplacentally or if maternal status is unknown.
- Infants born to HBsAg-positive mothers should be tested for HBsAg and antibody to HBsAg 1–2 months after completion of at least three doses of the HepB vaccine, at age 9–18 months.

These recommendations must be read with the footnotes that follow. For those who fall behind or start late, provide catch-up vaccination at the earliest opportunity as indicated by the green bars in Figure 1. To determine minimum intervals between doses, see the catch-up schedule (Figure 2). School entry and adolescent vaccine age groups are shaded in gray.

Vaccine	Birth	1 mo	2 mos	4 mos	6 mos	9 mos	12 mos	15 mos	18 mos	19-23 mos	2-3 yrs	4-6 yrs	7-10 yrs	11-12 yrs	13-15 yrs	16 yrs	17-18 yrs
Hepatitis B[1] (HepB)	1st dose	◄---- 2nd dose ----►			◄-------------------- 3rd dose --------------------►												
Rotavirus[2] (RV) RV1 (2-dose series); RV5 (3-dose series)			1st dose	2nd dose	See footnote 2												
Diphtheria, tetanus, & acellular pertussis[3] (DTaP: <7 yrs)			1st dose	2nd dose	3rd dose		◄-------- 4th dose --------►					5th dose					
Haemophilus influenzae type b[4] (Hib)			1st dose	2nd dose	See footnote 4		3rd or 4th dose, See footnote 4										
Pneumococcal conjugate[5] (PCV13)			1st dose	2nd dose	3rd dose		◄-------- 4th dose --------►										
Inactivated poliovirus[6] (IPV: <18 yrs)			1st dose	2nd dose	◄-------------------- 3rd dose --------------------►							4th dose					
Influenza[7] (IIV)					Annual vaccination (IIV) 1 or 2 doses							Annual vaccination (IIV) 1 dose only					
Measles, mumps, rubella[8] (MMR)					See footnote 8		◄-------- 1st dose --------►					2nd dose					
Varicella[9] (VAR)							◄-------- 1st dose --------►					2nd dose					
Hepatitis A[10] (HepA)							◄-------- 2-dose series, See footnote 10 --------►										
Meningococcal[11] (Hib-MenCY ≥6 weeks; MenACWY-D≥9 mos; MenACWY-CRM ≥2 mos)			See footnote 11											1st dose		2nd dose	
Tetanus, diphtheria, & acellular pertussis[12] (Tdap:≥7 yrs)														Tdap			
Human papillomavirus[13] (HPV)														See footnote 13			
Meningococcal B[11]														See footnote 11			
Pneumococcal polysaccharide[5] (PPSV23)												See footnote 5					

Range of recommended ages for all children
Range of recommended ages for catch-up immunization
Range of recommended ages for certain high-risk groups
Range of recommended ages for non-high-risk groups that may receive vaccine, subject to individual clinical decision making
No recommendation

NOTE: The above recommendations must be read along with the footnotes of this schedule.

FIGURE 6-1. **Recommended Immunization Schedule for Children and Adolescents Aged 18 Years or Younger—United States, 2017.** (Source: Centers for Disease Control and Prevention. https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html.)

CONTENT

Adsorbed recombinant hepatitis B surface antigen proteins.

SIDE EFFECTS

- Pain at injection site.
- Fever >99.9°F (37.7°C) in 1–6%.

CONTRAINDICATIONS

- Anaphylactic reaction to vaccine, yeast, or another vaccine constituent.
- Infants <2 kg.

DIPHTHERIA, TETANUS, AND ACELLULAR PERTUSSIS (DTaP)

- Minimum age: 6 weeks.
- Given IM at 2, 4, and 6 months, and a fourth dose between 15 and 18 months of age.
- The fourth dose may be administered as early as age 12 months; **provided** 6 months between third and fourth doses.
- Administer the final dose at age 4–6 years.
- DT without pertussis vaccine can be used in children <7 years of age if pertussis vaccine is contraindicated.
- TDaP is administered at age 10–12.

CONTENT

- DTaP is diphtheria and tetanus toxoids with acellular pertussis.
- DTP contains a whole-cell pertussis.

SIDE EFFECTS

- Erythema, pain, and swelling at injection site.
- Fever >100.4°F (38°C).
- Crying ≥ 1 hour.
- Severe side effects (more common with DTP, rare with DTaP): crying >3 years; hypotonic-hyporesponsive episode; seizures; fever >40.5°C.

CONTRAINDICATIONS

- Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component
- Encephalopathy not attributable to another cause within 7 days of a prior dose of pertussis vaccine.

PRECAUTIONS

- Seizure disorder or seizures within 3 days of receiving a previous dose of DTaP.
  - Poorly controlled or new-onset seizures: Defer pertussis immunization until seizure disorder is well controlled and progressive neurologic disorder is excluded.
  - Personal or family history of febrile seizures. Give DTaP and antipyretics around the clock for 24 hours after immunization.
- Temperature of 40.5°C (104.8°F) within 48 hours after immunization with previous dose of DTaP.
- Collapse or shock like state (hypotonic-hyporesponsive episode within 48 hours of receiving a previous dose of DTaP).
- Persistent inconsolable crying lasting >3 hours within 48 hours of receiving a previous dose of DTaP.
- Guillain-Barre syndrome within 6 weeks after a prior dose.

HAEMOPHILUS INFLUENZAE TYPE B (HIB)

- Minimum age: 6 weeks.
- Given IM at 2, 4, and 6 months of age, then again between 12 and 15 months of age.

CONTENT

Consists of a capsular polysaccharide antigen conjugated to a carrier.

SIDE EFFECTS

Erythema, pain, and swelling at injection site in 25%.

CONTRAINDICATIONS

Anaphylactic reaction to vaccine or vaccine constituent.

MEASLES, MUMPS, AND RUBELLA

> A 12-month-old boy is due for his vaccines in the middle of October. His mother mentions that he developed a skin rash as well as some respiratory problems 1 month prior after she fed him eggs for the first time. He is due for MMR, varicella, and influenza vaccines. *Think: Egg allergy* and the vaccines that are contraindicated: influenza vaccine, yellow fever vaccine. MMR can be given safely to children with egg allergy.

- Minimum age: 12 months.
- First dose given subcutaneously (SC) at 12–15 months of age, and second dose at 4–6 years of age.
- Second dose may be given at any time after 4 weeks from first dose if necessary.
- Must be at least 12 months old to ensure a sufficient response.

> **EXAM TIP**
>
> MMR is a live virus vaccine.

CONTENT

Composed of live attenuated viruses.

SIDE EFFECTS

- Fever >102.9°F (39.4°C) 6–12 days after immunization can last up to 5 days in 10%.
- Transient rash in 5%. May occur 1–6 weeks after vaccination.
- Febrile seizures and encephalopathy with MMR vaccine are rare. Transient thrombocytopenia may occur 2–3 weeks after vaccine in 1/40,000.
- Swollen lymph nodes.
- Pain or stiffness in joints.

CONTRAINDICATIONS

- Anaphylactic reaction to prior vaccine.
- Anaphylactic reaction to neomycin or gelatin.
- Immunocompromised states.
- Pregnant women.

PRECAUTIONS

- Recent intravenous immunoglobulin (IVIg) administration requires delaying vaccinations by 11 months.
- Throbocytopenia or history of thrombocytopenic purpura, however, benefits outweigh risks.

INACTIVATED POLIOVIRUS VACCINE (IPV)

- Minimum age: 6 weeks.
- Given IM or SQ at 2 and 4 months, then again between 6 and 18 months, then a fourth between 4 and 6 years of age.
- The final dose should be administered on or after the fourth birthday and at least 6 months following the previous dose.
- If four doses are administered prior to age 4 years, a fifth dose should be administered at age 4–6 years.
- OPV is given orally. No longer used in the United States.

CONTENT

- IPV contains inactivated poliovirus types 1, 2, and 3.
- Live oral poliovirus vaccine (OPV) contains live attenuated poliovirus types 1, 2, and 3.

SIDE EFFECTS

- Vaccine-associated paralytic polio (VAPP) with OPV in 1/760,000.
- Local reactions, fever.

CONTRAINDICATIONS

- Anaphylaxis to vaccine or vaccine constituent.
- Anaphylaxis to streptomycin, polymixin B, or neomycin.

VARICELLA

- Minimum age: 12 months.
- Given SC between 12 and 18 months of age; second dose between 4 and 6 years (may be administered before age 4, provided at least 3 months have elapsed since the first dose).
- Susceptible persons >13 years of age must receive two doses at least 4 weeks apart.

CONTENT

Cell-free live attenuated varicella virus.

SIDE EFFECTS

- Erythema and swelling in 20–35%.
- Fever in 10%.
- Varicelliform rash in 1–4%.

CONTRAINDICATIONS

- Anaphylactic reaction to vaccine, neomycin, or gelatin.
- Patients with altered immunity, including corticosteroid use for > 14 days.
- Patients on salicylate therapy. Avoid salicylates for 6 weeks after vaccine administration.
- Pregnant women.
- Recent blood product or IG administration (defer at least 11 months).

INFLUENZA VACCINE (SEASONAL)

- Minimum age: 6 months (quadrivalent inactivated influenza vaccine [TIV]); 2 years (live attenuated influenza vaccine) [LAIV]).

EXAM TIP

An all-IPV schedule is recommended in the United States to prevent VAPP (vaccine-associated paralytic polio). Under certain circumstances, OPV may be used.

EXAM TIP

OPV is contraindicated in immunodeficiency disorders or when household contacts are immunocompromised.

EXAM TIP

Varicella vaccine contains live virus.

WARD TIP

LAIV is no longer available because of inefficacy.

- Given IM to children >6 months of age yearly beginning in autumn, usually between October and mid-November (two doses 1 month apart for the first time).
- All children should receive this vaccine, especially high-risk children.
- Caution! LAIV should not be given to children aged 2–4 years who have had wheezing in the past 12 months.

CONTENT

- Contains four virus strains, usually both type A and type B based on the expected prevalent influenza strains for the coming winter.
- Children <9 years of age should receive the "split" vaccine only.
- Children receiving vaccine for the first time should receive 2 doses 1 month apart in order to obtain a good response.

SIDE EFFECTS

- Pain, swelling, and erythema at injection site.
- Fever may occur, especially in children <24 months of age.
- In children >13 years of age, fever may occur in up to 10%.
- Guillain-Barré syndrome, if given at the same time as PCV13 and/or DTaP.

CONTRAINDICATIONS

Severe allergic reaction (e.g., anaphylaxis) after a previous dose of any IIV or LAIV or to a vaccine component, including egg protein.

PRECAUTIONS

- Moderate or severe acute illness with or without fever.
- History of GBS within 6 weeks of previous influenza vaccination.
- Persons whose egg allergy reaction is limited to hives only may receive RIV (if age 18–49) or, with additional safety precautions, IIV.9

PNEUMOCOCCUS (CONJUGATE VACCINE)

- Minimum age: 6 weeks for pneumococcal conjugate vaccine (PCV), 2 years for pneumococcal polysaccharide vaccine (PPSV).
- Babies receive three doses (shots) 2 months apart starting at 2 months, and a fourth dose when they are 12–15 months old.
- Also given to high-risk children ≥ 2 years of age.
- PCV is recommended for all children aged younger than 5 years. Administer one dose of PCV to all healthy children aged 24–59 months who are not completely immunized for their age.
- Administer PPSV ≥2 months after last dose of PCV to children aged 2 years or older with certain underlying medical conditions, including a cochlear implant.

CONTENT

- The older PPV-23 vaccine (not indicated under age 2) contains the purified capsular polysaccharide antigens of 23 pneumococcal serotypes. The PPV-23 is usually reserved for high-risk children.
- The newer PCV-13 is the conjugate vaccine described above.

SIDE EFFECTS

- Erythema and pain at injection site.
- Anaphylaxis reported rarely.
- Fever and myalgia are uncommon.

WARD TIP

It is especially important to vaccinate for influenza those with asthma, chronic lung disease, cardiac defects, immunosuppressive disorders, sickle cell anemia, chronic renal disease, and chronic metabolic disease.

WARD TIP

Influenza vaccine does not cause the disease. The vaccine has been associated with an ↑ risk of Guillain-Barré syndrome (GBS) in older adults, but no such cases have been reported in children.

WARD TIP

Chemoprophylaxis against influenza is recommended as an alternative means of protection in those who cannot be vaccinated.

WARD TIP

The pneumococcal vaccine helps to protect against meningitis, bacteremia, pneumonia, and otitis media caused by serotypes of *Streptococcus pneumoniae*.

CONTRAINDICATIONS

- For PCV13, severe allergic reaction (e.g., anaphylaxis) after a previous dose of PCV7 or PCV13 or to a vaccine component, as well as to any vaccine containing diphtheria toxoid.
- For PPSV23, severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component.

HEPATITIS A VACCINE

- Minimum age: 12 months.
- Administer to all children aged 1 year (12–23 months).
- Administer two doses at least 6 months apart.
- Recommended for older children who live in areas where vaccination programs target older children, who are at ↑ risk for infection, or for whom immunity against hepatitis A is desired.
- are <24 months of age

HUMAN PAPILLOMAVIRUS (HPV)

- May be given between age 9 and 26 years to both girls and boys.
- Three dose series, with second dose 2 months after the first dose and the third dose 6 months after the first dose.
- Contains nine strains of HPV.

SIDE EFFECTS

Pain, swelling, dizziness, syncope.

MENINGOCOCCAL VACCINE

- Available against groups A, C, Y, W-135.
- New vaccine available against group B.
- All children receive tetravalent conjugate vaccine (MCV-4) at age 11, booster at age 16.
- Minimum age: 2 years for meningococcal conjugate vaccine (MCV4) and meningococcal polysaccharide vaccine (MPSV4).
- Administer MCV4 to children aged 2–10 years with:
    - Persistent complement component deficiency.
    - Anatomic or functional asplenia.

SIDE EFFECTS

- Localized erythema and pain.
- Fever.
- Headache.
- Fatigue.

CONTRAINDICATION

Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component.

PRECAUTION

History of Guillain-Barré syndrome.

ROTAVIRUS VACCINE

- Minimum age: 6 weeks.
- Administer the first dose at age 6–14 weeks (maximum age: 14 weeks 6 days). Vaccination should not be initiated for infants aged 15 weeks 0 days or older.

- The maximum age for the final dose in the series is 8 months 0 days.
- If Rotarix rotavirus vaccine is administered at ages 2 and 4 months, a dose at 6 months is not indicated.

CONTRAINDICATION

SCID.

PRECAUTIONS

Preexisting chronic gastrointestinal disease, history of intussusception, spina bifida, or bladder exstrophy.

SIDE EFFECTS

Diarrhea, intussusception.

RESPIRATORY SYNCYTIAL VIRUS (RSV)

- Palivizumab (synagis) is a monoclonal antibody used for prophylaxis against infections with RSV.
- Given IM once a month at the beginning of RSV season, usually beginning in October and ending in March.
- Who should receive the vaccine:
    - Children <2 years of age with chronic lung disease who have required medical therapy 6 months before the anticipated RSV season.
    - Children born at 32 weeks' gestation or earlier with other risk factors for lung disease.
    - Infants born <29 weeks, if less than 12 months old at the start of the RSV season.
    - Infants born 29 to <32 weeks, if <6 months at the start of the RSV season.
    - Infants born at 32–35 weeks who are <3 months at the start of the RSV season and who are likely to have increased RSV exposure (child care exposure or siblings <5 years old).
    - Infants with congenital abnormalities of the airway or neuromuscular disease.
    - Infants with hemodynamically significant cyanotic or acyanotic congenital heart disease.

TUBERCULOSIS (TB)

- Children at risk include:
    - Children living in a household with an adult who has active tuberculosis or has a high risk of contracting TB.
    - Children infected with HIV or another condition that weakens the immune system.
    - Children born in a country that has a high prevalence of TB.
    - Children visiting a country where TB is endemic and who have extended contact with people who live there.
    - Children from communities that generally receive inadequate medical care.
    - Children living in a shelter or living with someone who has been in jail.
- The Mantoux test contains five tuberculin units of purified protein derivative (PPD).

SCREENING

- Asymptomatic children at high risk for tuberculosis should be screened with a PPD test annually.
- Interpretation: See Table 6-1.

WARD TIP

Ask the following questions to determine the need for a PPD:
- Has a family member or contact had tuberculosis disease?
- Has a family member had a positive tuberculin skin test?
- Was your child born in a high-risk country (countries other than the United States, Canada, Australia, New Zealand, or Western European countries)?
- Has your child traveled (had contact with resident populations) to a high-risk country for more than one week?

TABLE 6-1.   Guidelines for Determining a Positive Tuberculin Skin Test Reaction

INDURATION > 5 MM	INDURATION > 10 MM	INDURATION > 15 MM
HIV-positive persons	Recent arrivals (< 5 years) from high-prevalence countries	Persons with no risk factors for TB
Recent contacts of TB case	Injection drug users	
Fibrotic changes on chest radiograph consistent with old TB	Residents and employees[a] of high-risk congregate settings: prisons and jails, nursing homes and other health care facilities, residental facilities for AIDS patients, and homeless shelters	
Patients with organ transplants and other immunosuppressed patients (receiving the equivalent of > 15 mg/d prednisone for > 1 month)	Mycobacteriology laboratory personnel	
	Persons with clinical conditions that make them high risk: silicosis, diabetes mellitus, chronic renal failure, some hematologic disorders (e.g., leukemias and lymphomas), other specific malignancies (e.g., carcinoma of the head or neck and lung), weight loss of > 10% of ideal body weight, gastrectomy, jejunoileal bypass	
Children < 5 years of age are considered to have a positive PPD if the measurement is > 5 mm and < 10 mm	Children < 4 years of age or infants, children, and adolescents exposed to adults in high-risk categories	

[a] For persons who are otherwise at low risk and are tested at entry into employment, a reaction of > 15 mm induration is considered positive.

(Reproduced with permission from the American Thoracic Society. Diagnostic standards and classification of tuberculosis in adults and children, Am J Respir Crit Care Med. 2000 Apr;161(4 Pt 1):1376–1395.)

- The QuantiFERON®-TB Gold test (QFT-G) is a newer alternative for detection of TB, approved by the U.S. Food and Drug Administration (FDA) in 2005.
  - Advantages:
    - Requires a single patient visit to draw a blood sample.
    - Results can be available within 24 hours.
    - Does not boost responses measured by subsequent test, which can happen with tuberculin skin tests (TSTs).
    - Is not subject to reader bias that can occur with TSTs.
    - Is not affected by prior BCG (bacille Calmette-Guérin) vaccination.
  - Disadvantages:
    - Blood samples must be processed within 12 hours after collection while white blood cells are still viable.
    - Limited data in children <17 years of age, among persons recently exposed to *Mycobacterium tuberculosis*, and in immunocompromised persons.
    - Errors in collecting or transporting blood specimens or in running and interpreting the assay can ↓ the accuracy of QFT-G.
    - Limited data on the use of QFT-G to determine who is at risk for developing TB disease.

Medications

Only 25% of Food and Drug Administration (FDA)-approved drugs have been approved for pediatric use.

DIFFERENCES BETWEEN CHILDREN AND ADULTS

ABSORPTION

- Infants have thinner skin; therefore, topical substances can more likely cause systemic toxicity.

- Children do not have the stomach acidity of adults until age 2, and gastric emptying time is slower and less predictable, → ↑ absorption of some medications.

DISTRIBUTION

- Less predictable in children.
- Total body water ↓ from 90% in infants to 60% in adults.
- Fat stores are similar to adults in term infants, but much less in preterm infants.
- Newborns have smaller protein concentration, therefore less binding of substances in the blood.
- Infants have an immature blood–brain barrier.

METABOLISM

Infants metabolize some drugs more slowly or rapidly than adults and may create a different proportion of active metabolites.

ELIMINATION

Kidney function ↑ with age, so younger children may clear drugs less efficiently.

DOSAGE

Pediatric medications are generally dosed by milligrams per kilogram (mg/kg).

Poisoning

EPIDEMIOLOGY

More often accidental in younger children and suicide gestures or attempts in older children/adolescents.

SIGNS AND SYMPTOMS

See Table 6-2.

PREVENTION

- Childproof home, including cabinets and containers.
- Store toxic substances in their original containers and out of children's reach.
- Supervise children appropriately.
- Have poison control center number easily accessible.

MANAGEMENT

- Frequently, ingested substances are nontoxic, but if symptoms arise or there is any question, a poison control center should be contacted.
- History:
  - Precise name of product (generic, brand, chemical—bring container or extra substance/pills).
  - Estimate amount of exposure, time of exposure.
  - Progression of symptoms.
  - Other medical conditions (e.g., pregnancy, seizure disorder).
- Gastric decontamination: Emesis (induced by syrup of ipecac) and gastric lavage remove only one third of stomach contents and are not generally recommended, though the combination of the latter with activated charcoal may be most effective.

TABLE 6-2. "Toxidromes," Symptoms, and Some Causes

ANTICHOLINERGIC	CHOLINERGIC	EXTRAPYRAMIDAL	HYPER-METABOLIC	OPIATES	WITHDRAWAL	SYMPATHO-MIMETIC
Hyposecretion, thirst, urinary retention	Hypersecretion Muscle fasciculation, weakness	Tremor, rigidity	Fever Tachycardia	CNS depression	Abdominal cramps, diarrhea	Hyperthermia, hypertension, tachypnea
Flushed skin, dilated pupils			Hyperpnea Restlessness Convulsions	Dilated pupils Hypothermia Hypotension	Lacrimation, sweating	Dilated pupils
Tachycardia, respiratory insufficiency	Bronchospasm, arrhythmias		Metabolic acidosis		Tachycardia, restlessness	Psychosis, convulsions
Delirium, hallucinations	Convulsions, coma				Hallucinations	
Belladonna	Organo-phosphates (insecticides)	Haloperidol	Salicylates	Lomotil	Cessation of:	Amphetamines
Some mushrooms		Metoclopramide		Propoxyphene Heroin	Alcohol Benzodiazepines	Cocaine Theophylline
Antihistamines	Some mushrooms			Methadone		Caffeine
Tricyclic antidepressants				Codeine	Barbiturates	
	Black widow spider bites			Morphine Demerol	Opiates	
	Tobacco					

- Activated charcoal is effective for absorbing many drugs and chemicals, though it does not bind heavy metals, iron, lithium alcohols, hydrocarbons, cyanide. It may be used in conjunction with cathartics such as sorbitol or magnesium sulfate.
- Dilution of stomach contents with milk has limited value except in the case of ingestion of caustic materials.
- Skin decontamination: Remove clothing, use gloves, flood area with water for 15 minutes, use other mild material such as petroleum or alcohol to remove substances not removed by water.
- Ocular decontamination: Rinse eyes with water, saline, or lactated Ringer's for > 15 minutes; consider emergency ophthalmologic exam.
- Respiratory decontamination: Move to fresh air; bronchodilators may be effective, inhaled dilute sodium bicarbonate may help acid or chlorine inhalation.
- Antidotes: See Table 6-3.
- Treat seizures, respiratory distress/depression, hemodynamics, and electrolyte disturbances as they arise.

TABLE 6-3. Drug Toxicities

Drug	Signs and Symptoms	Treatment/Antidote
Sulfonamides	Kernicterus in infants	
Chloramphenicol	Gray baby syndrome—vomiting, ashen color, cardiovascular collapse	
Quinolones	May cause cartilage defects in children	
Tetracycline	Gray enamel of permanent teeth, affects bone growth (avoid in children < 9 years old)	Not necessary unless massive ingestion
Salicylate	Reye syndrome—hepatic injury, hypoglycemia, vomiting—in children with viral illnesses Hypermetabolic	
Acetaminophen	Generalized malaise, nausea, vomiting Latent period Jaundice and bleeding (direct hepatocellular necrosis) Metabolic acidosis, renal and myocardial damage, coma	*N*-acetylcysteine (Mucomyst)
Tricyclic antidepressants	Anticholinergic Widened QRS, flattened T waves	Intubation and activated charcoal if altered sensorium Sodium bicarbonate IV
Prednisone	Growth retardation Cataracts	
Organophosphates	Cholinergic	Atropine Pralidoxime
Heavy metals (e.g., arsenic, mercury, lead, chromium, copper, gold, nickel, zinc)		Dimercaprol Dimercaptosuccinic acid (succimer, DMSA), EDTA
Iron	Abdominal pain, vomiting	Deferoxamine
Methanol, ethylene glycol	Intoxication	Ethanol
	Blindness (methanol)	Fomepizole
Benzodiazepines	Sedation	Flumazenil (recommended only in cases of iatrogenic overdose)
Opiates	Respiratory depression Pinpoint pupils	Naloxone
Anticholinergics	"Mad as a hatter; Dry as a bone; Blind as a bat; Red as a beet; Hot as Hades"	

Adolescence

- Adolescence comprises the ages between 10 and 21 years.
- The most common health problems seen in this age group include unintended pregnancies, sexually transmitted diseases (STDs), mental health disorders, physical injuries, and substance abuse.

PREVENTION

- Be on the lookout for adolescents at high risk for health problems, including physical, mental, and emotional health.
- Screen for depression. Suicide is the third leading cause of death in adolescents. Depression in the adolescent can manifest as irritability, anger, new drug use, and drop-off in school performance.
- Look for:
    - Decline in school performance, excessive school absences, cutting class.
    - Frequent psychosomatic complaints.
    - Changes in sleeping or eating habits.
    - Difficulty in concentrating.
    - Signs of depression, stress, or anxiety.
    - Conflict with parents.
    - Social withdrawal.
    - Sexual acting-out.
    - Conflicts with the law.
    - Suicidal thoughts, preoccupation with death.
    - Substance abuse.

SCREENING

- Routine health care should involve audiometry and vision screening, blood pressure checks, exams for scoliosis.
- Breast and pelvic exams in females may also be necessary, and self-exams should be emphasized.
- Likewise, examination for scrotal masses is necessary in males with emphasis on self-examination.
- STDs (**gonorrhea and chlamydia**), including HIV should be considered in those adolescents with high-risk behaviors. Counsel sexually active adolescents on contraception and protection against STDs.
- Screen with Pap smears within 3 years of the onset of sexual activity or at 21 years of age.
- Adolescents who are engaged in one risk-taking activity such as smoking cigarettes are at greater risk for experimenting with drugs and alcohol.
- Mental health screening at each yearly visit.

PHYSICAL EXAM

- Sexual maturity should be assessed at each visit.
- Assess for scoliosis at each visit until Tanner stage 5 is achieved.

PREGNANCY

EPIDEMIOLOGY

- In 2014, a total of 249,078 babies were born to women aged 15–19 years, for a birth rate of 24.2 per 1,000 women in this age group. This is another historic low for U.S. teens and a drop of 9% from 2013(CDC).

CONTRACEPTION

EPIDEMIOLOGY

Among U.S. high school students surveyed in 2015:
- 41% had ever had sexual intercourse.
- 30% had had sexual intercourse during the previous 3 months, and, of these
- 43% did not use a condom the last time they had sex.
- 14% did not use any method to prevent pregnancy.
- 21% had drunk alcohol or used drugs before last sexual intercourse (CDC).

RISK FACTORS

Factors associated with early sexual activity include poor academic performance, lower expectations for education, poor perception of life options, low school grades, and involvement in other high-risk behaviors such as substance abuse.

FORMS OF CONTRACEPTION

- Abstinence, condoms (male and female), diaphragm, cervical cap, spermicides, or some combination of these.
- Hormonal methods include oral contraceptive pills and injectable or implantable hormones, and hormone patches.
- Intrauterine devices are not recommended for adolescents because of the ↑ risk of sexually transmitted infections.

COMBINATION ORAL CONTRACEPTIVES

Usually consist of either 50, 35, 30, or 20 μg of an estrogenic substance such as mestranol or ethinyl estradiol plus a progestin.

SIDE EFFECTS

- Short-term effects may include nausea and weight gain.
- Other possible effects include thrombophlebitis, hepatic adenomas, myocardial infarction, and carbohydrate intolerance.

POTENTIAL BENEFITS

Long-range benefits may include ↓ risks of benign breast disease and ovarian disease.

HIV/AIDS

See the Infectious Disease chapter.

EPIDEMIOLOGY

- HIV/AIDS is the sixth leading cause of death among adolescents aged 15–24 years.
- One half of all new infections in the United States occur in people younger than 25 years of age.

SCREENING

Screening should include adolescents with risk factors such as previous STD, unprotected sex, practicing insertive or receptive anal sex, trading sex for money or drugs, homelessness, intravenous drug or crack cocaine use, being the victim of sexual abuse.

EXAM TIP

An ↑ in the number of years of schooling for a woman delays the age at which a woman marries and has her first child.

WARD TIP

Adolescents who smoke may ↑ their risk for side effects from oral contraceptives.

Child Abuse

DEFINITION

Child maltreatment encompasses a spectrum of abusive actions, and lack of action, that result in morbidity or death. Forms of child abuse include:
- Physical abuse
- Sexual abuse
- Neglect

RISK FACTORS

- Parental risk factors:
    - Low socioeconomic status.
    - Mother's age (young).
    - History of being abused as a child.
    - Alcoholism, substance abuse, psychosis.
    - Social isolation.
- Child risk factors:
    - Children with special needs, handicapped children (chronic illness, congenital malformation, mental retardation).
    - Prematurity.
    - Age <3 years.
    - Nonbiologic relationship to the caretaker.
    - "Difficult" children.
- Family and environmental factors:
    - Unemployment.
    - Intimate partner violence.
    - Poverty.

PHYSICAL ABUSE

Suspect if:
- Injury is unexplained or unexplainable.
- Injury is inconsistent with mechanism suggested by history.
- History changes each time it is told.
- There are repeated "accidents."
- There is a delay in seeking care.

Skin Manifestations

Bruises
- Most common manifestation of physical abuse
- Suspicious if:
    - Seen on nonambulatory infants.
    - Have geometric pattern (belt buckles, looped-cord marks).

Burns
- Suspicious if:
    - Involve both hands or feet in stocking-glove distribution or buttocks with sharp demarcation line (forced immersion in hot water).
    - Cigarette burns—if nonaccidental, usually full-thickness, sharply circumscribed.
    - "Branding" injuries (inflicted by hot iron, radiator cover, etc).
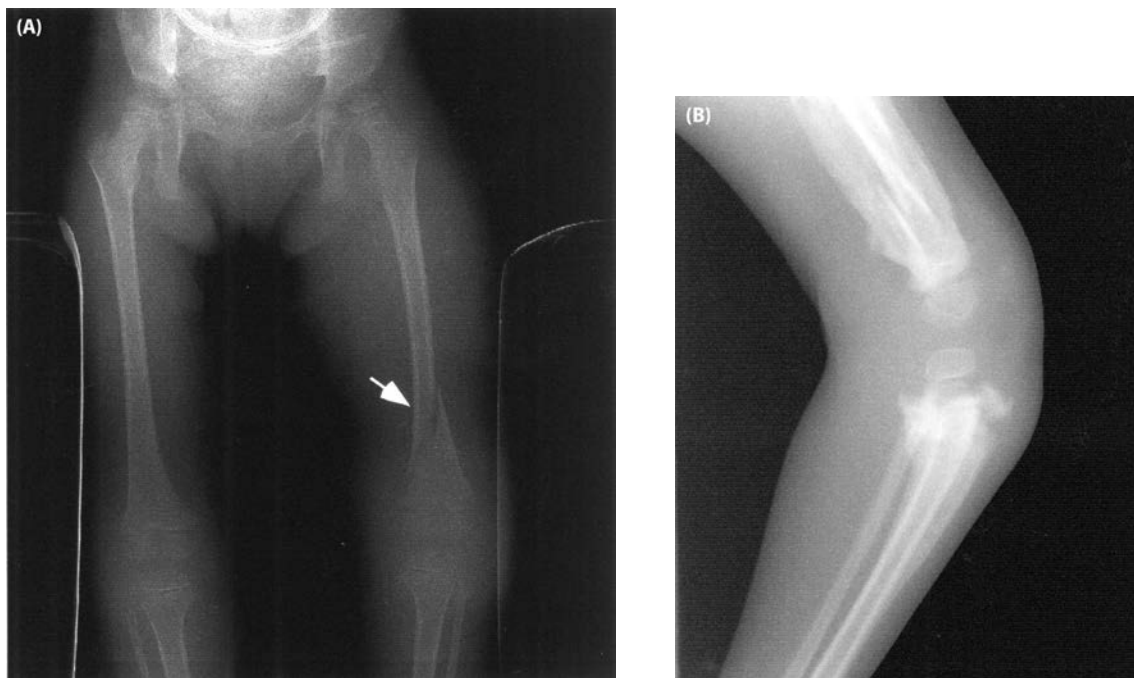
FIGURE 6-2. **(A)** Spiral fracture (arrow) of the femur in a nonambulatory child, consistent with nonaccidental trauma. **(B)** Same child 2 months later. Note the exuberant callus formation at all the fracture sites in the femur and proximal tibia and fibula.

Skeletal Injuries

Suspicious if:
- **S**piral fractures of lower extremities in nonambulatory children (see Figure 6-2A and B).
- **P**osterior rib fractures (usually caused by squeezing the chest).
- Fractures of different **A**ges.
- **M**etaphyseal "chip" fractures (usually caused by wrenching).
- **M**ultiple fractures.
- Scapular and clavicle fractures.

Central Nervous System (CNS) Injuries

- Most common cause of death in child abuse: "Shaken baby syndrome."
- Occurs due to violent shakes and slamming against mattress or wall while an infant is held by the trunk or upper extremities.
- Findings include:
  - **R**etinal hemorrhages.
  - **S**ubdural hematoma (from rupturing of bridging veins between dura mater and brain cortex).
- Symptoms include:
  - Lethargy or irritability
  - Vomiting
  - Seizures
  - Bulging fontanelle

ABDOMINAL INJURIES

- Second most common cause of death in child abuse.
- Usually no external marks. Most commonly, liver or spleen is ruptured.
- Symptoms include vomiting, abdominal pain or distention, shock.

EXAM TIP

CNS injuries suspicious of abuse: "**M**others, **R**efuse **S**haking!" (**M**etaphyseal fractures, **R**etinal hemorrhages, **S**ubdural hematoma)

WARD TIP

Epiphyseal-metaphyseal injury is virtually diagnostic of physical abuse in an infant, since an infant cannot generate enough force to fracture a bone at the epiphysis.

WARD TIP

Shaken baby syndrome can mimic meningitis or sepsis.

SEXUAL ABUSE

- Includes genital, anal, oral contact; fondling; and involvement in pornography.
- Most common perpetrators—fathers, stepfathers, mother's boyfriend(s) (adults known to child).
- Suspect if:
  - Genital trauma.
  - STDs in small children.
  - Sexualized behavior toward adults or children.
  - Unexplained decline in school performance.
  - Runaway.
  - Chronic somatic complaints (abdominal pain, headaches).
- Symptoms include:
  - May be totally absent.
  - Tears/bleeding in female or male genitalia.
  - Anal tears or hymenal tears (not very reliable symptoms).

EVALUATION OF SUSPECTED ABUSE

Physical Abuse

- Bleeding disorders must be ruled out in case of multiple bruises.
- X-ray skeletal survey (skull, chest, long bones) in children < 2 years of age (to look for old/new fractures).
- Computed tomographic (CT) scans of the head/abdomen as indicated.
- Ophthalmology consult.

Sexual Abuse

- Sexual abuse includes *any* sexual activity (nonconsensual and consensual) between an adult and a child.
- Cultures for STDs, test for presence of sperm, if indicated (usually within 72 hours of assault).

MANAGEMENT

- If abuse is suspected, it must be reported to child protective services (CPS) (after medical stabilization, if needed).
- All siblings need to be evaluated for abuse, too (up to 20% of them might have signs of abuse).
- Disposition of the child (i.e., whether to discharge the patient back to parents or to a CPS worker if medically cleared) has to be decided by CPS in conjunction with treating physician.
- Family must receive intensive intervention by social services and, if needed, legal authorities.
- *Remember*: If sent back to abusive family without intervention, up to 5% of children can be killed and up to 25% seriously reinjured.

NEGLECT

DEFINITION

- Neglect is the most common form of reported abuse.
- Neglect to meet nutritional, medical, and/or developmental needs of a child can present as:
  - Failure to thrive.
  - Poor hygiene (severe diaper rash, unwashed clothing, uncut nails).

WARD TIP

Children too young to talk about what has happened to them (generally younger than 2) should have a complete skeletal survey if you suspect abuse.

WARD TIP

A child who presents with multiple fractures at multiple sites and in various stages of healing should be considered abused until proven otherwise.

WARD TIP

Management of abuse:
  Suspect
  ↓
  Report
  ↓
  Disposition
  ↓
  Family counseling

- Developmental/speech delay.
- Delayed immunizations.
- Not giving treatment for chronic conditions.

MANAGEMENT

If nonorganic (i.e., due to insufficient feeding) failure to thrive is suspected:
- Patient should be hospitalized and given unlimited feedings for 1 week; 2 oz/24 hours of weight gain is expected.
  - All suspected cases of neglect must be reported to CPS.

MUNCHAUSEN SYNDROME BY PROXY

DEFINITION

- Parent/caregiver either simulates illness, exaggerates actual illness, or induces illness in a child.
- Psychiatrically disturbed parent(s) gain satisfaction from attention and empathy from hospital personnel or their own family because of problems created.

EPIDEMIOLOGY

- Affected children are usually < 6 years old.
- Parent (usually mother) has some medical knowledge.

SIGNS AND SYMPTOMS

- Vomiting (induced by ipecac).
- Chronic diarrhea (from laxatives).
- Recurrent abscesses or sepsis (usually polymicrobial, from injecting contaminated fluids).
- Apnea (from choking the child).
- Fever (from heating thermometers).
- Bloody vomiting or diarrhea (from adding blood to urine or stool specimens).

DIAGNOSIS

Diagnosis is difficult, but is initiated by removing child from parent via hospitalization. Usually, child without access to parent will have all/most symptoms resolved; testing will also usually be normal.

MANAGEMENT

- Admission to the hospital for observation, possibly using hidden video cameras.
- All cases of suspected Munchausen syndrome by proxy must be reported to CPS.

SUDDEN INFANT DEATH SYNDROME (SIDS)

DEFINITION

- Sudden death of an infant (< 1 year old) that remains unexplained after thorough case investigation, autopsy, and review of the clinical history.
- SIDS is one of the leading causes of death of infants.

ETIOLOGY

Apnea hypothesis.

> **EXAM TIP**
>
> Baron von Munchausen was an 18th-century nobleman who became famous because of his incredible stories, which included travel to the moon and flying atop a cannonball over Constantinople, as well as visiting an island made of cheese. His name became a synonym for gross confabulations.

DIAGNOSIS

Difficult to differentiate from intentional harm.

PREVENTION

- There has been a vast ↓ in the number of cases since the trend of having infants sleep on their backs (supine).
- The number one preventive measure to date is parental education, though the use of cardiorespiratory monitoring in the home is being debated.
- Limiting passive smoke exposure.
- Do not use soft bedding, pillows, stuffed animals, loose blankets.
- Co-sleeping with the parent increases the risk.

Congenital Malformations and Chromosomal Anomalies

It is important for all pediatricians in all fields to recognize signs and symptoms of congenital disorders, including dysmorphologic features. It is also important to involve genetics in the patient's care for appropriate screening and treatment of conditions associated with genetic syndromes, genetic testing, if available and appropriate, and counseling regarding siblings and possible future offspring of the patient. It is estimated that 2–4% of infants are born with some type of birth defect. While in many cases, the cause is unknown, most birth defects are caused by genetic or environmental factors or a combination of the two (multifactorial).

Environmental Factors

> An infant born to a mother from Puerto Rico is found to have microcephaly with ventriculomegaly and intracranial calcifications noted on CT scan of the brain. Think **congenital ZIKA infection** if mother is from an endemic area or has symptoms suggestive of Zika infection including fever, rash, conjunctivitis, or arthralgias during her pregnancy.

- Maternal infection: TORCH (toxoplasma, rubella, cytomegalovirus, herpes), syphilis, etc., and Zika virus must be considered in endemic areas.
- Maternal nutritional status: iodine deficiency (hypothyroidism, cretinism), folate deficiencies (neural tube defects), diabetes mellitus, etc.
- Maternal teratogen exposure: including medications like phenytoin, valproic acid, warfarin, lithium, etc., as well as exposures to alcohol, tobacco, pesticides, etc., during pregnancy.

Genetic Factors

Chromosomal abnormalities fall into numerical or structural abnormalities and can include single gene defects, parental imprinting, and molecular cytogenetics.
- Numerical abnormalities:
  - Trisomy: an extra chromosome is present as in Down syndrome (Trisomy 21).
  - Monosomy: a missing chromosome as in Turner syndrome (XO).
- Structural abnormalities:
  - Translocations: anomalies in which a whole or part of a chromosome is inappropriately joined with another chromosome.
  - Deletions and duplications: can also occur with various whole chromosomes or chromosomal segments (Table 7-1).

Trisomy Syndromes

TRISOMY 21 (DOWN SYNDROME)

> A female infant has slanted palpebral fissures, epicanthal folds, and some delayed development. *Think: Down syndrome.*
> This is a classic description of an infant with Down syndrome. The clinical features include flat facial profile and oblique palpebral fissures, and epicanthic folds are usually evident at birth. It is also a leading cause of severe mental retardation in children. It is the most common chromosomal disorder.

T A B L E   7 - 1 . **Types of Genetic Transmission**

AUTOSOMAL-DOMINANT CONDITIONS	AUTOSOMAL-RECESSIVE CONDITIONS	X-LINKED-RECESSIVE CONDITIONS
If parent is affected, risk in offspring is 50%	Recurrence risk for parents with an affected child 25% 1:4	Males are affected, heterozygous females are normal or have mild manifestations
Vertical transmission, people in every generation are affected	Less variability among affected persons	Inheritance is diagonal through maternal side
Variable expressivity	Inheritance is horizontal, siblings can be affected, skips generations	Female carrier has a 50% chance that each daughter will be a carrier and 50% chance that each son will be affected
Both male and female can pass on the abnormal gene	Frequently associated with enzyme defects	
Often related to structural abnormality of a protein	Increased risk with consanguinity	Ex: Duchenne and Becker muscular dystrophy, hemophilia A and B, G6PD
Ex: Marfan's, NF type 1, hereditary spherocytosis	Ex: Cystic fibrosis	

♟ A 33-week-gestation male infant born to a 40-year-old mother was noted to have facial dysmorphism with depressed nasal bridge, wide-spaced eyes, low hairline, and low-set ears. He was also noted to have a single palmar crease in both hands. At 2 hours of life he was noted to have bilious emesis, and an abdominal x-ray was obtained, as shown in the figure (see Figure 7-1). What is the diagnosis and management of this infant?

The infant described was born to a mother with advanced maternal age (>35 years) and features consistent with trisomy 21 (Down syndrome). X-ray is notable for the classic double-bubble sign, which is pathognomonic for duodenal atresia. Management includes surgical repair of the duodenal atresia and also to confirm the diagnosis of trisomy 21 by chromosome analysis.

✋ **WARD TIP**

Look for "double-bubble sign" in a plain abdominal radiograph (see Figure 7-1).
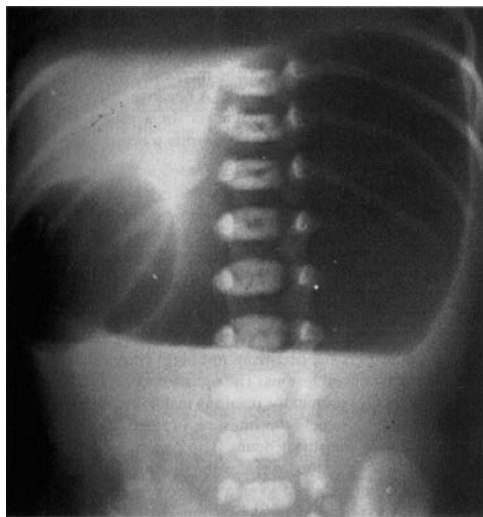
F I G U R E   7 - 1 . **Duodenal atresia.** Gas-filled and dilated stomach show the classic "double-bubble" appearance of duodenal atresia. Note no distal gas is present. (Reproduced, with permission, from Rudolph CD, et al (eds). *Rudolph's Pediatrics*, 21st ed. New York: McGraw-Hill, 2002: 1403.)

Palpebral fissure
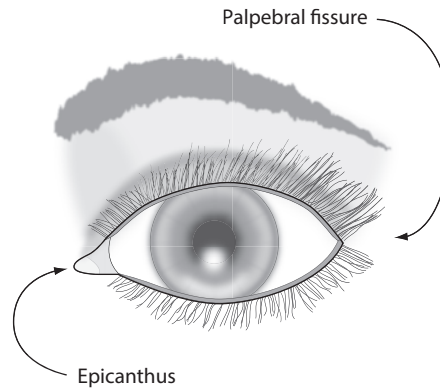
Epicanthus

FIGURE 7-2. Location of epicanthus and palpebral fissure. In Down syndrome, there are epicanthal folds and upwardly slanted palpebral fissures. (Reproduced, with permission, from Rudolph CD, et al (eds). Rudolph's Pediatrics, 21st ed. New York: McGraw-Hill, 2002: 1403).

- Extra copy of the genetic material on chromosome 21.
- Most common malformation syndrome.
- Most common chromosome disorder.
- Most common genetic cause of moderate mental retardation.

ETIOLOGY

- Ninety-five percent complete trisomy (meiotic nondisjunction of homologous chromosomes).
- Four percent Robertsonian translocation (to chromosome 14).
- One percent mosaicism.

EPIDEMIOLOGY

One in 600 births.

RISK FACTORS

Advanced maternal age.

SIGNS AND SYMPTOMS

- More than 100 different physical signs can be present.
- Varying degrees of mental retardation (most with IQs between 35 and 70).
- Generalized hypotonia (of central nervous system [CNS] origin; most meet major motor milestones at 2× normal age).
- Balding scalp hair pattern.
- Upslanted eyes with epicanthal folds (see Figure 7-2).
- Flat nasal bridge.
- Prominent tongue.
- Extra neck skin folds (sometimes visible on prenatal ultrasound).
- Transverse single palmar creases.
- Small ears.
- Short stature.
- Joint laxity.
- Hypoplastic nipples.
- Brushfield spots on irises.
- Subendocardial cushion defect (atrial/ventricular septal defect [ASD/VSD], atrioventricular [AV] canal).
- Duodenal atresia, Hirschsprung's disease, imperforate anus.
- Hypothyroidsim.
- Amyloid plaques and neurofibrillary tangles in brain—early onset dementia.
- ↑ risk of leukemia (acute lymphocytic leukemia [ALL], acute myelogenous leukemia [AML], acute megakaryocytic leukemia).

WARD TIP

Patients with Down syndrome develop Alzheimer's dementia early, around age 35.

WARD TIP

Think of duodenal atresia in a newborn with Down syndrome presenting with bilious vomiting.

- ↑ risk of neonatal leukemoid reactions.
- Atlantoaxial instability becomes an issue later in life.
- Most males with Down syndrome are sterile but some females have been able to reproduce.

DIAGNOSIS

- Prenatal diagnosis can be made via amniocentesis or chorionic villus sampling.
- Maternal serum α-fetoprotein (AFP) is ↓.
- Low maternal serum unconjugated estriol level.
- Elevated maternal beta-human chorionic gonadotropin (β-hCG).

TREATMENT

- Early childhood intervention to maximize social and intellectual capacity.
- Life skills training.
- Surgery for correction of cardiac and duodenal defects.
- At risk for atlantoaxial dislocation and cervical cord compression.
- ↑ risk for leukemia and respiratory tract infections.
- Yearly screening for thyroid disease.

TRISOMY 18 (EDWARDS SYNDROME)

ETIOLOGY

- Most common type is complete trisomy.
- Small percentage are due to mosaicism.

EPIDEMIOLOGY

One in 6000 live births; second most common trisomy.

SIGNS AND SYMPTOMS

- Prominent occiput.
- Low-set ears.
- Small mouth.
- Short sternum.
- Thumb and radius agenesis/hypoplasia.
- Camptodactyly (little finger fixed in flexion).
- Redundancy of cardiac valve leaflets.
- Hypertonia.
- Seizures.
- Rocker-bottom feet.

TREATMENT

- Supportive.
- Fifty percent die within first week of life. Most common cause of death is apnea.
- Five to ten percent survive beyond the first year.
- Those who survive are severely mentally retarded.

TRISOMY 13 (PATAU SYNDROME)

Higher frequencies in stillbirths and spontaneous abortions.

ETIOLOGY

- Seventy-five percent complete trisomy.
- Twenty-three percent Robertsonian translocation (to chromosome 14).
- Four percent mosaicism.

EPIDEMIOLOGY

- One in 10,000 live births.

SIGNS AND SYMPTOMS

- Holoprosencephaly (failure of telencephalon to divide into two hemispheres, resulting in large central ventricle; brain assumes configuration of a fluid-filled ball).
- Microphthalmia and other eye defects (coloboma, cyclops).
- Midline facial defects.
- Polydactyly.
- Scalp cutis aplasia.
- Cystic kidneys.
- VSD.

TREATMENT

- Supportive.
- Eighty percent die within first month; 5% survive past 6 months.

Sex Chromosome Anomalies

TURNER SYNDROME

A newborn infant has lymphedema of the hands and feet, extra skin folds at a short neck, widely spaced nipples, and ↓ femoral pulses. *Think: Gonadal dysgenesis (45,X) Turner syndrome,* and do a chromosomal analysis to confirm the diagnosis.

Many infants with Turner syndrome are recognized at birth due to the presence of edema of the hands and feet and loose skin folds at the nape of the neck. Coarctation of aorta may be present in up to 20%.

ETIOLOGY

45,XO—caused by a loss of part or all of an X chromosome.

EPIDEMIOLOGY

One in 2000–2500 live female births.

RISK FACTORS

Not related to advanced maternal age.

PATHOPHYSIOLOGY

Connective tissue disorder affecting fibrillin.

SIGNS AND SYMPTOMS

- Short stature.
- Webbed neck.
- Lymphedema of hands and feet.
- Coarctation of the aorta + biscuspid aortic valve.
- Small mandible.
- Congenital malformations of the renal/urinary system are present in 30–40%.
- Narrow maxilla and high arched palate.
- Epicanthal folds.

WARD TIP

Turner syndrome is the most common cause of primary amenorrhea.

WARD TIP

There are Turner syndrome–specific growth charts to monitor their growth.

- Impaired hearing (sensorineural).
- Delay in motor skill development with normal intelligence.
- Ovarian dysgenesis.
- Phenotypically female.
- Association with spontaneous abortion.
- Patients who have Y chromosome mosaicism have an increased risk of gonadoblastemia.

TREATMENT

- Growth hormone therapy starting in early childhood is recommended to maximize adult height.
- Replacement for secondary sex characteristic development.
- Monitor for autoimmune hypothyroidism.
- Refer to an endocrinologist for induction of puberty at an appropriate age.
- Lifelong hearing testing q1-5 years—tympanometry and audiology.
- Resection of any intra-abdominal gonads to prevent malignancy.

NOONAN SYNDROME

EPIDEMIOLOGY

- 1:1000-2500 live births
- Phenotypically similar to Turner syndrome but can affect both sexes.
- Mild facial dysplasia—hypertelorism, low-set ears.
- Pulmonary stenosis, hypertrophic cardiomyopathy, pectus excavatum.
- Girls with Noonan syndrome have normal XX chromosomes.
- Autosomal dominant.
- Mental retardation often present.
- Short stature can be treated with growth hormone.

KLINEFELTER SYNDROME

ETIOLOGY

- Presence of an extra X chromosome in males.
- 47,XXY most common.
- High yield: Most common cause of hypogonadism and infertility in males.

EPIDEMIOLOGY

One in 500 males.

RISK FACTORS

Advanced maternal age.

DIAGNOSIS

- Karyotyping of peripheral leukocytes.
- 10% diagnosed prenatally, diagnosis rarely made before puberty. (Prepubertal boys have a normal phenotype.)
- Most cases are diagnosed during evaluations for infertility or gynecomastia.

SIGNS AND SYMPTOMS

- Hypogonadism.
- Small testes but puberty occurs at the normal age.
- Most patients are phenotypically normal until puberty.

> **WARD TIP**
>
> There is a high association between Turner syndrome and coarctation of the aorta. Therefore, genetic testing for Turner syndrome should be performed in all girls diagnosed with coarctation!

- Azoospermia (absence of sperm).
- Tall stature (eunuchoid).
- Female hair distribution, gynecomastia.
- Learning disabilities.
- Delay of motor skill development.
- Presence of inactivated X chromosome (Barr body).
- Higher risk for cryptorchidism.

TREATMENT

- Administration of testosterone during puberty to improve secondary sex characteristics.
- Interventions for developmental delays/learning disabilities.
- Mastectomy can reduce risk of breast cancer and improve psychosocial outcomes.

Imprinting Disorders

Imprinting—different phenotype, same genotype.

ANGELMAN SYNDROME

ETIOLOGY

- Sixty percent due to **maternal** deletion 15q11–13 (see Prader-Willi syndrome).
- Forty percent have two normal paternal copies of chromosome 15.

EPIDEMIOLOGY

One in 20,000.

DIAGNOSIS

Methylation and chromosomal microarray.

SIGNS AND SYMPTOMS

- Happy, laughing disposition—previously known as the "happy puppet" or "marionette joyeuse" syndrome because of this, and stereotyped flapping of hands.
- Often, strikingly attractive children with lighter pigmentation than other family members (often blond-haired, blue-eyed).
- Profound intellectual disability.
- Microcephaly.
- Ataxia and tremors.
- Hypotonia (ataxia and hypotonia create the characteristic "puppet"-like gait).
- Epilepsy (80%) with characteristic electroencephalographic (EEG) findings of large amplitude slow-spike waves.
- Complete absence of speech.
- Unusual facies characterized by a large mandible and open-mouthed expression revealing tongue.
- Inappropriate laughter.

TREATMENT

- Supportive.
- Seizures are often refractory to anticonvulsant therapy.
- Normal life span.

EXAM TIP

The same chromosomal deletion causes Angelman syndrome and Prader-Willi syndrome. The only difference is that in Angelman syndrome the missing genetic material is maternal, and in Prader-Willi, paternal.

PRADER-WILLI SYNDROME

ETIOLOGY

- Genetic.
- Seventy-five percent **paternal** deletion 15q11–13 (see Angelman syndrome).
- Twenty-five percent maternal disomy.

EPIDEMIOLOGY

One in 15,000–20,000.

DIAGNOSIS

Testing is done in sequence, first with karyotype and methylation studies followed by FISH.

SIGNS AND SYMPTOMS

- Small hands and feet.
- Hypogonadism.
- Almond-shaped eyes.
- Thin upper lip.
- Hypotonia and poor feeding (in infancy) progressing to hyperphagia and obesity by childhood.
- Precocious puberty.
- Micropenis.
- Mild mental retardation.
- Sleep disturbances secondary to central/obstructive apnea.
- Lighter pigmentation than other family members.
- Significant behavioral problems (stubborn, manipulative, aggressive).
- Fluent speech.
- Obsessive/compulsive traits.

TREATMENT

- Strict diet and behavioral interventions to prevent obesity.
- Growth hormone to promote stature, and other timely hormone supplementation to promote secondary sex characteristics.
- Patients develop complications from obesity that limit their life span.
- Early prevention of obesity is the key to quality and quantity of life in these patients.

> **EXAM TIP**
>
> Neonatal hypotonia is one of the hallmarks of Prader-Willi Syndrome and is a clue to initiate testing.

> **EXAM TIP**
>
> Prader-Willi is the most common cause of syndromic obesity.

Molecular Cytogenetic Disorders

22Q11 SYNDROME

- Caused by deletion of a small piece of chromosome 22.
- Seen in DiGeorge syndrome (DGS), velocardiofacial syndrome.
- Occurs in 1 in 4000 births.
- Most common features include congenital heart defects (85%), palatal abnormalities, thymic aplasia, immune deficiency (defective T-cell function), hypocalcemia (parathyroid underdevelopment), characteristic facial features.
- Cardiac features include tetralogy of Fallot, interrupted aortic arch.
- 1% have complete absence of thymic tissue consistent with complete DGS which is a type of severe combined immunodeficiency (SCID). This is life-threatening if not corrected with immunoglobulin therapy.
- Detected by fluorescence in situ hybridization (FISH).
- Complete DGS may also be identified on newborn screening for SCID.

> **WARD TIP**
>
> DiGeorge syndrome can be distinguished from CHARGE syndrome which has a normal FISH, ocular colobomas, and genitourinary anomalies in addition to the cardiac and facial anomalies.

FRAGILE X SYNDROME

ETIOLOGY

Due to ↑ number of repeated nucleotide sequences (CGG).

EPIDEMIOLOGY

- One in 2000 births.
- Male-to-female ratio: 2:1.

RISK FACTORS

Family history.

SIGNS AND SYMPTOMS

- Mental retardation.
- Attention deficit disorder.
- Macroorchidism in boys.
- Protruding ears, macrocephaly, triangular, elongated facies, flat malar bones.
- Shyness, autistic behavior, avoidance of eye contact.

Congenital Anomalies

POLYDACTYLY

DEFINITION

- Presence of more than five fingers or toes, which may be rudimentary to fully developed.
- Incidence: 2 per 1000 live births.

ETIOLOGY

- May occur as an isolated defect (whether genetic, toxic, or mechanical) or in conjunction with syndromes such as:
  - Ellis–van Creveld syndrome: with congenital heart disease.
  - Bardet-Biedl syndrome: with obesity, pigmentary retinopathy, mental retardation, hypogonadism, and renal failure.
  - Meckel-Gruber syndrome: Triad of occipital encephalocele, large polycystic kidneys, and postaxial polydactyly. Associated abnormalities include oral clefts, genital anomalies, CNS malformations, fibrosis of the liver, and pulmonary hypoplasia.

DIAGNOSIS

Observation, x-ray, fetal sonogram.

TREATMENT

Surgery, usually at 1 year of age.

SYNDACTYLY

DEFINITION

Webbing or fusing of two or more fingers or toes. May be bony and/or cutaneous. Often looked for between the second and third toes.

PATHOPHYSIOLOGY

Failure of cell apoptosis between digits during development.

TREATMENT

Surgery.

CRANIOSYNOSTOSIS

DEFINITION

- Premature closing of one or more cranial sutures due to abnormalities of skull development.
- Can be primary skull/bone defect or a result of failure of brain growth.
- Syndromic craniosynostosis in 20%.
- Most common: Apert syndrome and Crouzon syndrome.

ETIOLOGY

May occur alone or in conjunction with syndromes such as:
- Apert syndrome.
- Chotzen syndrome.
- Pfeiffer syndrome.
- Carpenter syndrome.
- Crouzon syndrome.

SIGNS AND SYMPTOMS

Early closure of fontanels and sutures.

COMPLICATIONS

- Hydrocephalus.
- ↑ intracranial pressure (ICP).
- Developmental delay.

TREATMENT

- Craniotomy to prevent intracranial and ophthalmologic complications.
- Multidisciplinary approach—genetics, psychology, pediatrics, surgery, neurology.
- Genetic counseling.
- Long-term follow-up.

AMNIOTIC BAND SEQUENCE

DEFINITION

- Fibrous strands of membrane stretching across chorionic cavity.
- Form of disruption.

EPIDEMIOLOGY

Not associated with problems in future pregnancies.

ETIOLOGY

- Spontaneous.
- Associated with abdominal trauma.
- May be associated with chorionic villus sampling (CVS).

PATHOPHYSIOLOGY

Caused by early amnion rupture and leakage of chorionic fluid.

SIGNS AND SYMPTOMS

- May be innocent and not cause any harm to the fetus.
- Can → limb or other body part constriction or amputation (amniotic band syndrome).
- May be associated with oligohydramnios and ↓ fetal movement.

DIAGNOSIS

Ultrasound.

TREATMENT

- Most bands disappear on their own, not appearing on follow-up ultrasound.
- Rarely, necrosis distal to vascular occlusion might necessitate immediate surgical release.

CLEFT PALATE/LIP

DEFINITION

- Spectrum of defects of the upper lip, philtrum, and hard and soft palates.
- Cleft lip, cleft palate, or both.
- Unilateral or bilateral.

EPIDEMIOLOGY

- Fourth most common birth defect.
- Incidence of orofacial clefting is 1 in 700 live birth.
- Occur more often in infants of Asian, Latino, or Native American descent.
- More common in males.

ETIOLOGY

- Teratogens—ethanol, anticonvulsants, steroids, chemotherapy, maternal vitamin A excess.
- Gestational factors—maternal diabetes, amniotic bands.
- Chromosomal abnormalities.
- Idiopathic (majority).

PATHOPHYSIOLOGY

- Clefting of lip and anterior (primary) palate due to defect in fusing of both maxillary processes with the frontonasal process during weeks 5 and 6.
- Clefting of posterior (secondary) palate due to defect in fusion of palatal shelves during weeks 7 and 8.

SIGNS AND SYMPTOMS

Can affect feeding, speech, illness (colds and ear infections), teething, hearing, and emotional coping.

DIAGNOSIS

Physical exam of lips, palate, and oropharynx.

TREATMENT

- Infants with cleft palate may require assistance with feeding.
- Surgical repair of lip within first months of life, palate around 1 year of life; potential for final repairs and scar revisions in adolescence.

- Cleft team can include plastic and oral surgeons; geneticist; ear, nose, and throat (ENT) specialist; dentist; speech pathologist; audiologist; social worker or psychologist; and nurse coordinator.
- Genetic counseling.

OMPHALOCELE

DEFINITION

Herniation of abdominal contents (usually only intestine, though can include liver and/or spleen) through umbilical root, which is covered only by peritoneum.

EPIDEMIOLOGY

- May be associated with other congenital defects, including chromosomal anomalies, heart defects, and diaphragmatic hernia.
- Association: Beckwith-Wiedemann syndrome (omphalocele, macrosomia, hypoglycemia), trisomies 13 and 18.

DIAGNOSIS

Some may be detected on prenatal ultrasounds.

TREATMENT

- Until any other, more serious conditions have been taken care of, the extruded contents are covered.
- Serial reductions of intestines back into abdomen until skin closure is possible.

OLIGOHYDRAMNIOS

DEFINITION

- Abnormally small amount of amniotic fluid (amniotic fluid index [AFI] <5.0 cm or single pocket of fluid <2 cm).
- Volume <500 mL = oligohydramnios.
- Complicates 1–5% of pregnancies.

ETIOLOGY

- Premature rupture of membranes (PROM).
- Intrauterine growth retardation (IUGR).
- Postdates pregnancy.
- Renal anomalies (e.g., bilateral renal agenesis, multicystic dysplastic kidneys, posterior urethral valves).
- Other congenital anomalies (e.g., aneuploidy).
- Placental abruption.
- Twin-twin transfusion.
- Iatrogenic—nonsteroidal prostaglandin synthetase inhibitors, first-trimester chorionic villus sampling, second-trimester amniocentesis; amniotic fluid level may return to normal.
- Idiopathic.

PATHOPHYSIOLOGY

Amniotic fluid is regulated by fetal urine, as well as fetal oral secretions and respiratory secretions. Any process disrupting this exchange of fluid can lead to pathological amniotic fluid levels. Low amniotic fluid restricts fetal movement leading to multiple physical abnormalities.

WARD TIP

In a normal pregnancy, there is approximately 600 mL of amniotic fluid surrounding the baby at 40 weeks' gestation.

WARD TIP

Amniotic fluid volume ↓ as gestational age advances beyond 32 or 34 weeks' gestation.

WARD TIP

Isolated third-trimester oligohydramnios is not necessarily associated with poor perinatal outcome.

WARD TIP

Oligohydramnios becomes most evident after 20 weeks of gestation.

WARD TIP

Pulmonary hypoplasia is the most serious complication of oligohydramnios.

COMPLICATIONS

- Fetal demise.
- Pulmonary hypoplasia.
- Facial deformities.
- Skeletal deformities (e.g., compressed thorax, twisted feet).

POTTER SYNDROME

- Potter syndrome specifically refers to bilateral renal agenesis, though other renal anomalies → oligohydramnios have also used the eponym.
- Potter syndrome includes pulmonary hypoplasia, skeletal anomalies, and characteristic facies (sloping forehead; flattened nose; recessed chin; and low-set, floppy ears).
- It is incompatible with neonatal life.
- Death occurs due to pulmonary hypoplasia.

DIAGNOSIS

- Amniotic fluid index (AFI)—sum of the maximum vertical pocket of amniotic fluid in each quadrant of the uterus.
- Best to use average of three readings.

TREATMENT

- Depends on etiology.
- First goal is to remove the inciting cause or correct the underlying problem (e.g., discontinue prostaglandin inhibitor, place a shunt).
- Measures to prepare fetus for possible premature birth (corticosteroids and antibiotics for PROM).
- Antepartum testing to determine appropriate time for delivery in IUGR.

HYPOSPADIAS

DEFINITION

Improper location of urethral meatus, not at tip of penis, but on underside of penis, even as far back as the scrotum.

ETIOLOGY

Hereditary—if father has, there is a 20% chance that child will.

SIGNS AND SYMPTOMS

- Curvature of penis downward; foreskin "hooding."
- Potentially may have to sit down to urinate.

DIAGNOSIS

Clinical diagnosis, though radiologic studies may be necessary if other congenital defects are present.

TREATMENT

- Surgical correction to extend urethra to end of penis before 18 months of age and chordae repair if sexual function will be affected by bent erect penis.
- May require more than one operation.
- Beware of postoperative bleeding, infections, stenosis, and fistulae.

Overgrowth Syndromes

BECKWITH-WIEDEMANN SYNDROME

- Omphalocele, macroglossia, macrosomia.
- Predisposition to tumor development during first 8 years of life.
- Occurs sporadically, familial transmission in 15% of cases.

KLIPPEL-TRENAUNAY SYNDROME

Capillary/venous malformations and limb overgrowth.

PROTEUS

Asymmetric disproportionate overgrowth of soft tissue and bone, cutaneous/visceral mixed vascular malformations.

An infant born with a prenatally diagnosed omphalocele, who is found after birth to have macroglossia. The infant was referred for genetic testing which reveal hypomethylation of the IC2 critical regions of chromosome 11p15 consistent with the diagnosis of Beckwith-Wiedemann syndrome.

Metabolic Disease

Inborn Errors of Metabolism

DEFINITION

Inherited biochemical disorders.

PATHOPHYSIOLOGY

Mutations affecting proteins involved in the many metabolic pathways of the body. Typically result in deficiency of enzyme production or build-up of toxic metabolites, or both.

EPIDEMIOLOGY

Disorders involving deficiencies of enzymes are often autosomal recessive (please see noted exceptions in this chapter).

SIGNS AND SYMPTOMS

- Often normal at birth, but can show signs early, including metabolic acidosis, poor feeding, vomiting, lethargy, and convulsion.
- Mental retardation, organomegaly, unusual body odor, episodic decompensation.

DIAGNOSIS

- **Newborn metabolic screening:**
  - Standard in the United States: Allows for early detection and treatment and can potentially prevent serious consequences.
  - Panel of test varies state by state but phenylketonuria (PKU), hypothyroidism, galactosemia, and hemoglobinopathies are nearly universal.
  - Tandem mass spectrometry is the usual method used for screening.
  - The following conditions are screened in most states:
    - Galactosemia.
    - Hypothyroidism.
    - Hemoglobinopathy.
    - Tyrosinemia.
    - Biotinidase deficiency.
    - Congenital adrenal deficiency.
    - Maple syrup urine disease.
    - Homocystinuria.
    - Cystic fibrosis.
    - Medium-chain acyl-CoA dehydrogenase deficiency (MCAD).
    - Urea cycle defects.
- Classification:
  - Amino acid and urea cycle disorders:
    - Homocystinuria.
    - Maple syrup urine disease.
    - Phenylketonuria.
    - Tyrosinemia.
    - **Urea cycle** (arginase deficiency, argininosuccinic academia, citrullinemia, ornithine transport defect).
  - Fatty acid oxidation disorders:
    - Carnitine transport defect.
    - Citrullinemia.
    - Glutaric acidemia type 2.
    - Medium-chain acyl-CoA dehydrogenase deficiency.
  - Organic acid disorders:
    - 3-hydroxy-3-methyglutaryl-CoA lyase deficiency

WARD TIP

Medium-chain acyl-CoA dehydrogenase deficiency is the most common fatty acid oxidation disorder and may be associated with intermittent severe metabolic crises or sudden death.

TABLE 8-1. Newborn Screening of Amino Acid Disorders

DISORDER	SCREENING TEST	AGE OF TREATMENT	CONFIRMATORY TEST
Phenylketonuria (PKU)	Mass spectrometry	First weeks of life	Plasma phenylalanine and mutation testing
Tyrosinemia	Mass spectrometry	First weeks of life	Plasma amino acid profile and urine succinylacetone
Maple syrup urine disease (MSUD)	Mass spectrometry	First weeks of life	Plasma amino acid profile and allo-isoleucine

- ▪ Glutaric acidemia type I
- ▪ Isovaleric acidemia
- ▪ Methylmalonic acidemia
- ▪ Propionic acidemia
- ▪ Many can be detected in the neonatal period or infancy, and some are included in newborn screening (see Table 8-1).

TREATMENT

- ▪ Treatment varies but is often supportive/symptomatic.
- ▪ Frequently includes dietary modifications.
- ▪ Increasing availability of enzyme or gene-related treatment options.

Defects of Amino Acid Metabolism

See Table 8-2.

PHENYLKETONURIA (PKU)

DEFINITION

Inherited disorder of amino acid metabolism in which there is an impaired ability to metabolize the essential amino acid phenylalanine.

ETIOLOGY

Deficiency of phenylalanine hydroxylase (or its cofactor tetrahydrobiopterin— 2% of cases).

> ✋ **WARD TIP**
>
> Most fatty acid oxidation disorders present with hypoglycemia.

TABLE 8-2. Disorders of Amino Acid Metabolism

DISEASE	ACCUMULATION	DEFICIENCY	DISTINCTIVE FEATURE	
Phenylketonuria (PKU)	Phenylalanine and metabolites	Usually phenylalanine hydroxylase	Fair hair and skin, blue eyes, mousy odor	AR
Homocystinemia/ Homocystinuria	Homocystine, methionine	Usually cystathionine synthase	Ectopia lentis	AR
Maple syrup urine disease (MSUD)	Branched-chain amino acids: leucine, isoleucine, valine	Branched-chain ketoacid dehydrogenase	Odor of maple syrup in urine, sweat, cerumen	AR
Hartnup disease	Deficiency of neutral amino acids: tryptophan	Sodium-dependent amino acid transport system in renal tubules and intestines	Most are asymptomatic	AR

PATHOPHYSIOLOGY

- Accumulation of phenylalanine and its phenylketone metabolites disrupt normal metabolism and cause brain damage.
- Tyrosine becomes essential amino acid.

EPIDEMIOLOGY

- Autosomal recessive.
- One in 10,000–20,000 live births.
- Routinely screened for in the United States.

SIGNS AND SYMPTOMS

- Normal at birth.
- Severe mental retardation may develop at the end of 1 year (progressive and irreversible) if not treated early after birth.
- Hypopigmentation due to low tyrosine (fair hair and skin, blue eyes).
- Eczema, mousy/musty body odor, hypertonia.

DIAGNOSIS

- Screened in all newborns.
- Serum tested 72 hours after initiation of first protein feed (test may be negative prior to 72 hours).
- If not screened neonatally, diagnosis usually made at 4–6 months of age.
- Prenatal and carrier testing possible.

TREATMENT

- Limit dietary phenylalanine (e.g., in artificial sweeteners) and ↑ tyrosine; if started within first 10 days of life, infants can have normal intelligence.
- Strict dietary restriction during pregnancy.

HOMOCYSTINEMIA/HOMOCYSTINURIA

DEFINITION

Inherited disorder of amino acid metabolism in which homocysteine is present in greater than trace amounts in the urine.

ETIOLOGY

Most commonly a deficiency of cystathionine β-synthase, but can also be a defect of methylcobalamin formation or deficiency of methyltetrahydrofolate reductase (see Figures 8-1 and 8-2).

PATHOPHYSIOLOGY

Homocysteine is not remethylated to methionine (see Figure 8-1).

EPIDEMIOLOGY

Autosomal recessive (1 in 200,000 live births).

SIGNS AND SYMPTOMS

- Depends on particular enzyme deficiency.
- Most commonly normal at birth, with failure to thrive and developmental delay subsequently occurring.
- Shares several skeletal and ocular features with Marfan syndrome.
- Later, downward ectopia lentis, marfanoid body habitus without arachnodactyly, progressive mental retardation, vaso-occlusive disease, osteoporosis, or fair skin with malar flush can occur.
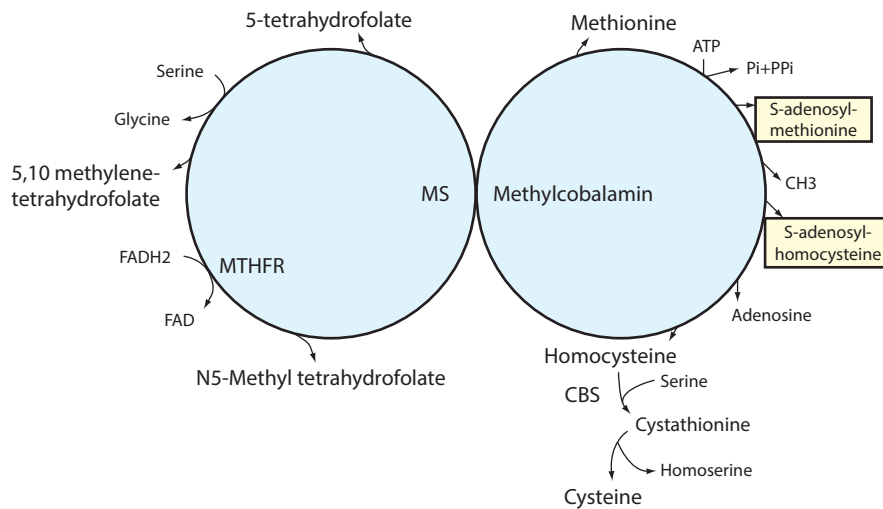
F I G U R E 8 - 1 . **Homocysteine pathway.**
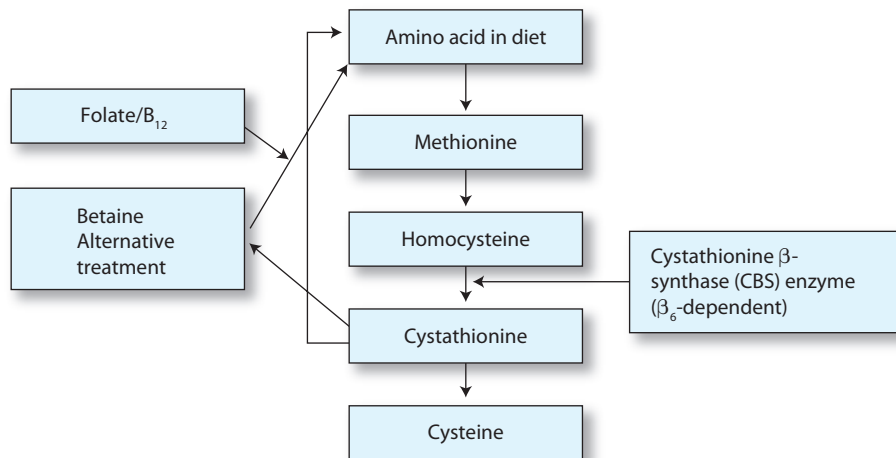
F I G U R E 8 - 2 . **Methionine metabolism.**

DIAGNOSIS

- Normal at birth; diagnosis usually made after 3 years of age.
- Elevated methionine and homocysteine in body fluids.
- Prenatal diagnosis possible.
- Marfan phenotype—differential diagnosis:
    - Homocystinuria: Marfanoid habitus, ectopia lentis, mental retardation, osteoporosis.
    - Ehlers-Danlos syndrome types 1 and 3: Marked joint hypermobility, mitral valve prolapse.
    - Stickler syndrome (hereditary arthro-ophthalmopathy): Tall stature, retrognathia, mitral valve prolapse, midfacial hypoplasia, retinal detachment.
    - Klinefelter syndrome: Marfanoid habitus, small testes and genitalia, learning difficulty.

TREATMENT

- Pyridoxine responsive form: 50% are this form and easily missed in the neonatal period. High-dose vitamin B_6.

> **EXAM TIP**
>
> Branched-chain amino acids are leucine, isoleucine, and valine.

- Pyridoxine unresponsive form: Restriction of methionine intake and supplementation of cysteine. (May require concurrent folic acid to show response.) Betaine can also play a role in this group.
- Other types may require vitamin B_{12} or methionine supplementation.

MAPLE SYRUP URINE DISEASE (MSUD) OR BRANCHED-CHAIN KETOACIDURIA

DEFINITION

Inherited disorder of branched-chain amino acid metabolism in which elevated quantities of leucine, isoleucine, valine, and corresponding oxoacids accumulate in the body fluids.

ETIOLOGY

Deficiency of branched-chain ketoacid dehydrogenase.

PATHOPHYSIOLOGY

Defect in the decarboxylation of leucine, isoleucine, and valine by a branched-chain ketoacid dehydrogenase.

EPIDEMIOLOGY

One in 250,000 live births in general population.

SIGNS AND SYMPTOMS

- Deficiency of different subunits of enzyme account for wide clinical variability.
- Poor feeding, vomiting in first week of life, proceeding to lethargy and coma.
- Developmental delay and poor myelination.
- Alternating hypertonicity and flaccidity, convulsions, hypoglycemia and metabolic acidosis.
- Odor of maple syrup in urine, sweat, cerumen (burnt sugar smell).

DIAGNOSIS

- Elevated plasma and urine levels if leucine, isoleucine, valine, and allo-isoleucine; ↓ plasma alanine.
- Urine precipitant test.
- Neuroimaging in the acute state shows cerebral edema.

TREATMENT

- Chronically, low branched-chain amino acid diet.
- Protein restriction in the first 2 weeks of life may lessen neurological damage.
- Frequent serum level monitoring.
- Acutely, intravenous administration of amino acids other than branched chain.
- Hemodialysis or peritoneal dialysis can save the patient's life in acidotic crisis, but liver transplantation can definitely treat MSUD.

HARTNUP DISEASE

DEFINITION

Inherited defect in transport of neutral amino acids by intestinal mucosa and renal tubules.

ETIOLOGY

Deficient activity of a sodium-dependent transport system.

PATHOPHYSIOLOGY

Deficiency of tryptophan results in the clinical manifestations.

EPIDEMIOLOGY

Autosomal recessive.

SIGNS AND SYMPTOMS

- Usually asymptomatic.
- Rarely, intermittent ataxia, cutaneous photosensitivity, episodic psychiatric changes.
- Marginal nutrition results in clinical manifestations in predisposed individuals.

DIAGNOSIS

- Aminoaciduria (neutral: alanine, serine, threonine, valine, leucine, isoleucine, phenylalanine, tyrosine, tryptophan, histidine).
- Normal plasma amino acid levels.

TREATMENT

Nicotinic acid/nicotinamide and a high-protein diet in symptomatic patients.

Defects of Lipid Metabolism—Lysosomal Storage Diseases

LIPIDOSES

See Table 8-3.

DEFINITION/ETIOLOGY/PATHOPHYSIOLOGY

Inherited deficiencies of lysosomal hydrolases cause lysosomal accumulation of sphingolipids in brain and viscera.

EPIDEMIOLOGY

Most are autosomal recessive.

SIGNS AND SYMPTOMS

Depends on site of abnormal accumulations:
- Nervous system: Neurodegeneration, ocular findings.
- Viscera: Organomegaly, skeletal abnormalities, pulmonary infiltration.

DIAGNOSIS

Measurement of specific enzymatic activity in leukocytes or cultured fibroblasts.

TREATMENT

- Usually no specific treatment.
- Supportive/symptomatic therapy.
- Gaucher disease: Recombinant enzyme.
- Krabbe disease: Hematopoietic stem cell transplant.

WARD TIP

Gaucher disease is the most common lysosomal storage disease (1 in 75,000). Splenomegaly is the most common presenting sign.

EXAM TIP

Fabry disease is X-linked recessive.

EXAM TIP

Gangliosidoses (e.g., GM1 and Tay-Sachs) have cherry-red spot on macula in 50% of cases, as does Niemann-Pick.

EXAM TIP

Hepatosplenomegaly occurs in the GM1 gangliosidoses and Sandhoff disease, but not in Tay-Sachs disease.

T A B L E 8 - 3 . Lysosomal Storage Diseases—Lipidoses

DISEASE	DEFICIENCY/ACCUMULATION	FEATURE	INHERITANCE
GM1 gangliosidoses	■ Deficiency of β-galactosidase ■ Accumulation of GM1 ganglioside	■ Infantile, juvenile, adult forms (multiple forms) ■ 50% cherry red spot on macula but clear cornea ■ Hepatosplenomegaly ■ Rashes, edema, psychomotor retardation ■ Coarse facial features, skeletal abnormalities ■ Blind and deaf by 1 year, death by 3–4 years of age ■ WBC with inclusions	Autosomal recessive
GM2 gangliosidoses	*Tay-Sachs disease:* ■ Deficiency of α subunit hexosaminidase A ■ Results in accumulation of GM2 ganglioside in brain *Sandhoff disease:* ■ Accumulation of GM2 ganglioside in brain and peripheral organs ■ Defect of β subunit hexoseaminidases A and B	■ Infantile and juvenile forms (multiple forms) ■ Diagnosis at 5–6 months, death by 3–5 years of age ■ Cherry red spot on macula but clear cornea ■ Hyperacusis (exaggerated startle response) ■ Froglike position ■ No organomegaly in Tay-Sachs ■ Hepatosplenomegaly in Sandhoff disease ■ Normal WBC	Autosomal recessive Ashkenazi Jews (Tay-Sachs)
Niemann-Pick disease (six subtypes)	■ Deficiency of sphingomyelinase ■ Accumulation of sphingomyelin and cholesterol in reticuloendothelial and parenchymal cells	■ 50% cherry red spot on macula in type A and normal in B and C types All types with clear cornea ■ Hepatosplenomegaly, neonatal jaundice ■ Diagnosis by 4 months, death by 3 years of age (infantile onset) ■ Varying neurologic signs/deterioration (depending on subtype) ■ Foam cells in bone marrow aspirates	Autosomal recessive Ashkenazi Jews
Gaucher disease (three types)	■ Deficiency of β-glucosidase ■ Accumulation of glucocerebroside in reticuloendothelial system	■ Type I is most common (Ashkenazi Jews) ■ Affects bone, liver, spleen, bone marrow, and brain (types II and III) ■ Pancytopenia ■ Bone fractures, pain, avascular necrosis ■ Gaucher cells in bone marrow —"crinkled paper" cytoplasm ■ Infantile form—rapid neurologic deterioration ■ Adult form—more common, normal life span ■ Treated with enzyme replacement	Autosomal recessive
Fabry disease	■ Deficiency of ceramide trihexosidase or α-galactosidase A ■ Accumulation of glycosphingolipids in vascular endothelium, nerves, and organs ■ Clinical onset in childhood and adolescence	Angiokeratomas (dark red punctate macules that do not blanch, occur in clusters, some become papules, distribution is bilateral and symmetric, navel and buttocks most common) and teleangiectasias ■ First sign is severe neuropathic limb pain ■ Asymmetric corneal deposits (cornea cloudy on slit lamp examination) ■ Progressive kidney failure (biopsy shows lipid) and hepatomegaly ■ Cardiac involvement with disease progression	X-linked recessive

TABLE 8-3. Lysosomal Storage Diseases—Lipidoses (*continued*)

DISEASE	DEFICIENCY/ACCUMULATION	FEATURE	INHERITANCE
Krabbe disease (globoid cell leukodystrophy)	■ Deficiency of galactosyl-ceramide β-galactosidase or galactocerebrosidase ■ Accumulation of ceramide galactose within lysosomes of brain white matter	■ Progressive central nervous system degeneration; symptoms present within first 6 months of life ■ Optic atrophy, spasticity, early death but clear cornea ■ Globoid cells in areas of demyelination (distended, multinucleated bodies found in basal ganglia, pontine nuclei, and cerebellar white matter) ■ Treatment: Hematopoietic stem cell transplant for infants prior to onset of neurologic symptoms	Autosomal recessive
Farber disease	■ Deficiency of ceramidase ■ Accumulation of ceramide in peripheral organs, joints, and lymph nodes	■ Normal at birth; clinical onset at 4 months of age and diagnosis at 1 year ■ Nodules (granulomas containing ceramide) on joints, vocal cords (hoarseness, respiratory complications) ■ Severe mental and motor retardation Clear cornea with cherry-red spot in 12% of cases	Autosomal recessive

MUCOPOLYSACCHARIDOSES

DEFINITION/ETIOLOGY/PATHOPHYSIOLOGY

Inherited deficiencies of lysosomal enzymes needed for the degradation of glycosaminoglycans (GAGs) resulting in widespread lysosomal storage of dermatan and heparan sulfates and severe clinical abnormalities. Keratan sulfates accumulate in other mucopolysaccharidoses not mentioned. See Table 8-4.

TABLE 8-4. Lysosomal Storage Diseases—Mucopolysaccharidoses

SYNDROME	DEFICIENCY	DISTINCTIVE FEATURES	INHERITANCE
Hurler syndrome (MPS I)	α-L-iduronidase	■ Severe, progressive; clinical onset at 1 year of age and death by 10 years of age ■ Mental retardation, heart disease, corneal clouding, organomegaly, coarse facies ■ Dysostosis multiplex, obstructive airway disease ■ Enlarged tongue, hearing loss, limited language	Autosomal recessive
Scheie syndrome (milder form of Hurler's)	α-L-iduronidase	■ Normal intelligence and relatively normal life span ■ Corneal clouding, stiff joints, aortic regurgitation	Autosomal recessive
Hunter syndrome (MPS I)	Iduronate 2-sulfatase	■ Mild to severe; clinical onset 1–2 year of age and death before 15 years in severe form ■ Dysostosis multiplex, mental retardation, organomegaly, coarse facies ■ Clear cornea but associated with retinitis and papilledema in severe cases	X-linked recessive

MPS, mucopolysaccharidosis.

Hunter syndrome is X-linked recessive.

WARD TIP

Dysostosis Multiplex
- Large dolichocephalic skull
- Thickened calvarium
- Ovoid vertebral bodies
- Flared iliac bones
- Shallow acetabulae
- Thickened clavicles
- Irregular widening of long bones

Epidemiology

Most are autosomal recessive.

Signs and Symptoms

- Normal at birth, diagnosis at 1+ years.
- "Gargoyle" cells containing lysosomes engorged with mucopolysaccharide.
- Excessive urinary excretion of GAGs.
- Progressive mental and physical deterioration.
- Coarse features.
- Corneal clouding.
- Stiff joints (abnormal hyalinization of collagen).
- Organomegaly.
- Skeletal abnormalities.

Diagnosis

- Detection of enzyme deficiency in leukocytes or cultured fibroblasts.
- Roentgenographic changes consistent with dystosis multiplex.
- Urinary excretion of dermatan and heparan sulfates.

Treatment

Supportive therapy. Hurler's can be treated with bone marrow transplant.

Defects of Carbohydrate Metabolism—Glycogen Storage Diseases

See Table 8-5.

VON GIERKE DISEASE

A 3-month-old, breast-fed infant has failure to thrive, severe hepatomegaly, thin extremities, fasting hypoglycemia, lipemia, and metabolic acidosis. *Think: von Gierke disease.*

von Gierke is an inherited disorder that affect glycogen metabolism. It is due to the deficiency of glucose-6-phosphatase, which results in accumulation of glucose-6-phosphate, which in turn causes ↑ glycolysis and lactic acidosis. It is characterized by growth retardation, hypoglycemia, hepatomegaly, hyperlipidemia, hyperuricemia, lactic acidemia, and seizure. In neonatal period, hypoglycemia and lactic acidosis are the common presentation. Hepatomegaly becomes evident by 3–4 months of age.

T A B L E   8 - 5 .   Glycogen Storage Diseases

Disease	Glycogen Accumulation	Deficiency	Type
von Gierke disease	Liver, kidney, and intestine	Glucose-6-phosphatase	I
McArdle disease	Skeletal muscle	Skeletal muscle glycogen phosphorylase	V
Pompe disease	Cardiac and skeletal muscle	α-1,4-glucosidase (acid maltase)	II

DEFINITION

Inherited disorder of glycogen metabolism characterized by deposition of glycogen in the **liver, kidney,** and **intestine.**

ETIOLOGY

Deficiency of glucose-6-phosphatase.

PATHOPHYSIOLOGY

Glycogen-to-glucose metabolism stops at glucose-6-phosphate.

EPIDEMIOLOGY

Autosomal recessive.

SIGNS AND SYMPTOMS

- Fasting hypoglycemia (due to impaired gluconeogenesis, glycogenolysis, and recycling of glucose through the glucose-6-phosphate to glucose system).
- Massive hepatomegaly.
- Elevated serum levels of lactate, uric acid, cholesterol, triglycerides.
- Renal complications (Fanconi syndrome, nephrocalcinosis, focal segmental glomerulosclerosis).
- Slow growth, diarrhea, bleeding disorders, hypotonia, and gout.
- Patients are at a high risk for hepatocellular carcinoma.

DIAGNOSIS

- Normal at birth; diagnosis usually at 5 months.
- Administration of epinephrine, glucagon, galactose, fructose, or glycerol does not provoke normal hyperglycemic response (may precipitate acidosis).
- DNA tests form common mutations.
- In cases where mutation testing is not easily done, enzyme measurements can confirm the diagnosis.
- Liver biopsy demonstrates accumulation of glycogen in cells.

TREATMENT

- Avoid fasting.
- Supportive therapy aimed at maintaining normal glucose levels.
- Nocturnal intragastric, frequent, high-carbohydrate meals are the mainstay of treatment up to 1–2 years age.
- After 2 years of age, snacks or nocturnal intragastric feedings of uncooked cornstarch may be sufficient.
- High-protein diet is not effective.
- Granulocyte colony–stimulating factors to combat neutropenia and inflammation.
- Allopurinol to lower urate levels, bicarbonate or potassium citrate for lactic acidosis.
- Liver transplant for refractory disease.

MCARDLE DISEASE

DEFINITION

Inherited disorder of glycogen metabolism characterized by deposition of glycogen in skeletal muscle.

ETIOLOGY

Deficiency of muscle glycogen phosphorylase (myophosphorylase).

WARD TIP

McArdle disease affects the **M**uscles.

EPIDEMIOLOGY

Autosomal recessive.

SIGNS AND SYMPTOMS

- Involves only skeletal muscles (accumulations of glycogen predominant in subsarcolemmal location).
- Temporary weakness and cramping of skeletal muscles during or after exercise.
- No rise in blood lactate during exercise.
- Characteristic "second wind" with initiation of fatty acid metabolism.
- Severe episodes can lead to myoglobinuria and concomitant renal failure.

DIAGNOSIS

- Asymptomatic during infancy. Presents in adolescence/early childhood.
- Muscle biopsy and assay show deficiency of enzyme.
- Myoglobinuria, serum creatine kinase always elevated (elevated CK at rest).

TREATMENT

- Dietary modification (high fat and protein); sucrose prior to aerobic exercise; proper "warm-up" period.
- Prognosis is good with sedentary lifestyle.

POMPE DISEASE

DEFINITION

Inherited disorder of glycogen metabolism characterized by deposition of glycogen in cardiac and skeletal muscle.

ETIOLOGY

Deficiency of acid α-1,4-glucosidase (acid maltase).

PATHOPHYSIOLOGY

- Generalized glycogenesis because the defect is in all cells.
- Results in inability to convert mannose to glucose.

EPIDEMIOLOGY

Autosomal recessive.

SIGNS AND SYMPTOMS

- Presents in the first 2 weeks of life with poor feeding, flaccid weakness, and cardiomegaly.
- Rapid, progressive cardiomyopathy with massive cardiomegaly, macroglossia, hypotonia, hepatomegaly; death by 1–2 years.
- Juvenile form milder, slowly progressive myopathy, little to no cardiac abnormality. Death usually secondary to respiratory failure.

DIAGNOSIS

- Electrocardiogram (ECG): May show shortened PR interval.
- Electromyogram (EMG).

TREATMENT

Enzyme replacement with recombinant α-glucosidase delays disease progression.

GALACTOSEMIA

A 2-week-old neonate has jaundice, hepatomegaly, and positive urinary-reducing substance. Odor of urine is normal. *Think: Galactosemia.*

Since galactosemia is included in the newborn screening, it is diagnosed before the symptoms develop. Jaundice, hepatomegaly, vomiting, lethargy, and feeding difficulties are the common initial presentation. Presence of a reducing substance in urine in infants with galactosemia who are ingesting lactose establishes the diagnosis.

DEFINITION

Inborn errors of carbohydrate metabolism that result in elevated galactose and metabolite levels in blood and urine.

ETIOLOGY

Three types:
- Classic: Absence of galactose-1-phosphate uridyltransferase (inability to process lactose/galactose).
- Others: Galactokinase, uridine diphosphate galactose-4-epimerase.

PATHOPHYSIOLOGY

- Ingestion of galactose $\rightarrow \uparrow$ concentrations in the blood and urine.
- Toxic substances, including galactitol, cause organ damage.

EPIDEMIOLOGY

- Autosomal recessive.
- One in 60,000.

SIGNS AND SYMPTOMS

- Cataracts (with oil-spot appearance), hepatosplenomegaly, mental retardation, sepsis (*E. coli*).
- Triad: **Liver failure** (jaundice and coagulation disorder), **renal tubular dysfunction** (glucosuria, aminoaciduria, and acidosis), and **cataract.**
- Most females with galactosemia suffer from ovarian failure.

DIAGNOSIS

- Should be considered in newborn, infant, or child if jaundice, hepatomegaly, vomiting, hypoglycemia, convulsions, lethargy, irritability, feeding difficulties, poor weight gain, diarrhea, aminoaciduria, cataracts, vitreous hemorrhage, hepatic cirrhosis, ascites, splenomegaly, or mental retardation are noted.
- Presence of reducing substance in urine after ingestion of human or cow's milk is suggestive.
- Routinely screened for in the United States (Table 8-6).

WARD TIP

When diagnosis of galactosemia is not made at birth, damage to the liver and brain become irreversible.

WARD TIP

Neonates with galactosemia are at ↑ risk for *Escherichia coli* sepsis.

WARD TIP

Elimination of galactose from diet in galactosemia does not ensure reversal of cataract formation.

TABLE 8-6. Screening for Galactosemia and Urea Cycle Defect

DISORDER	SCREENING	AGE OF TREATMENT	CONFIRMATORY TEST
Galactosemia	GALT enzyme measurement	First few days of life	GALT enzyme measurement, DNA mutations, galactose-1-P measurement
Urea cycle	Mass spectrometry	First few days of life	Plasma amino acid profile, DNA mutations

TREATMENT

- Exclude galactose and lactose from diet (example: dairy and breast milk).
- Soy-based formula.

FRUCTOSURIA

DEFINITION

Inborn errors of carbohydrate metabolism that result in elevated fructose and metabolite levels in blood and urine.

ETIOLOGY

Deficiency of fructokinase.

PATHOPHYSIOLOGY

- Enzyme is normally found in the liver, kidney, and intestine.
- Ingested fructose is not metabolized.

EPIDEMIOLOGY

Autosomal recessive.

SIGNS AND SYMPTOMS

- Asymptomatic until fructose introduced into diet.
- Fructosemia and fructosuria.

DIAGNOSIS

Presence of urinary-reducing substrate without clinical symptoms.

TREATMENT

None indicated.

Defects in Purine Metabolism

LESCH-NYHAN SYNDROME

DEFINITION

- An X-linked-recessive disorder of purine metabolism resulting in deposition of purines in tissues and subsequent clinical abnormalities.
- Up to 1% of patients with gout may have Lesch-Nyhan syndrome.

ETIOLOGY

Deficiency of **hypoxanthine–guanine phosphoribosyl transferase (HGPRT).**

SIGNS AND SYMPTOMS

- Delayed motor development.
- Extrapyramidal sign resulting in choreoathetosis at approximately 1 year of age.
- Spastic cerebral palsy, self-injurious behavior.
- Hyperuricemia, uricosuria, urinary tract calculi, nephropathy, tophi, gouty arthritis.

DIAGNOSIS

- Normal at birth; diagnosis usually made at 3 months when delayed motor development becomes apparent.

- Uric acid crystalluria may first be noted as orange crystals in the diaper during the first weeks of life.
- Serum uric acid levels.
- Gout generally does not develop until puberty.

TREATMENT

- No specific treatment; supportive therapy.
- Allopurinol to reduce serum uric acid levels.
- Prevention of self-injury.
- Death (due to infection or renal failure) in the second or third decade.

Familial Hypercholesterolemias

See Table 8-7.

TABLE 8-7. Familial Hyperlipidemias

DISORDER	LIPIDS	CLINICAL MANIFESTATIONS	TREATMENT	DEFICIENCY
Hypercholesterolemia (type II hyperlipoproteinemia)	■ Large elevations in serum cholesterol (>500 mg/dL) ■ Heterozygous form is common: ~1:500 ■ Homozygous form is very rare: ~1:1,000,000	■ Tendinous xanthomata ■ Early atherosclerotic cardiovascular disease (late childhood/early adulthood myocardial infarction)	■ Statins and cholestyramine for heterozygous form ■ Liver transplant for rare homozygous form	Genetic defect in low-density lipoprotein (LDL) receptor
Hyperchylomicronemia (type I hyperlipoproteinemia)	■ Accumulation of chylomicrons ■ Low/normal LDL ■ Serum grossly milky	■ Eruptive xanthomata ■ Periodic severe abdominal pain (pancreatitis) starting in infancy (colic) ■ No atherosclerotic disease	■ Very-low-fat diet may resolve xanthomatosis and reduce the risk of painful (and sometimes fatal) crises	Autosomal recessive (rarer than type II) Deficiency of lipoprotein lipase or cofactor apolipoprotein C-II
Dysbetalipoproteinemia (Type III)	■ Absent chylomicrons ■ Abnormal very-low-density lipoprotein (VLDL) and LDL ■ Moderately severe elevations of cholesterol and triglyceride (TG) levels ■ Cholesterol-to-TG ratio may equal 1	■ Planar xanthomata ■ Premature peripheral vascular disease and coronary artery disease	■ Planar xanthomata ■ Weight loss, diet, exercise ■ Adults with persistent elevations treated with fibric acid derivatives	Abnormal apolipoprotein E
Endogenous hypertriglyceridemia	■ ↑ VLDL	■ Obesity, glucose intolerance ■ Insulin resistance ■ Hyperinsulinemia ■ Hyperuricemia	■ Weight control ■ Dietary modification	Overproduction or reduced clearance of VLDL

Concepts in Hereditary Disease

- Complex heterozygosity: Different mutations in each gene allele—each individually "silent," but when combined produce clinical or biochemical manifestations.
- Consanguinity (children of first-degree relatives): ↑ risk for inherited disorders, as many are autosomal recessive.
- Sudden infant death syndrome (SIDS) or apparent life-threatening event (ALTE) may be the initial presentation of an inborn error of metabolism.
- Unexplained developmental delay may indicate an underlying metabolic disease.

Immunologic Disease

Immune System

■ **Primary lymphoid organs**—development of lymphocytes: Bone marrow, fetal liver, and spleen. Thymus: maturation of T cells.
■ **Secondary lymphoid tissue**—sites of antigen recognition: Lymph nodes, spleen, mucosal-associated lymphoid tissues (MALT), and gut-associated lymphoid tissues (GALT).
■ Maternal serum antibodies (immunoglobulin G [IgG]) transferred across the placenta protect the infant from birth until approximately 6 months of age, and totally disappear by 12–18 months of age. This leads to a physiologic nadir of serum antibodies at 6 months.
■ Maternal antibodies (IgA) are transferred to the child's intestinal tract through breast milk.
■ A child's IgG antibodies begin developing between 6 months and 1 year of age.
■ Children under the age of 2 years develop strong immune response to polysaccharide antigens in a vaccine (*Haemophilus influenzae*, pneumococcal) if they are conjugated to a protein carrier.

Hypersensitivity Reactions

See Table 9-1 for types of hypersensitivity reactions.
■ **Urticaria (hives):** Pale or reddened irregular, elevated itchy patches of skin.
■ **Angioedema:** Giant wheals caused by localized dilation and ↑ permeability of the capillaries in the deep dermis.
■ **Vesicle:** A collection of fluid underneath epidermis = blister <5 mm in diameter.
■ **Bulla:** Blister >5 mm in diameter with thin walls.

ANAPHYLAXIS

DEFINITION

A severe and potentially life-threatening systemic allergic IgE-mediated reaction caused by release of mediators from tissue mast cells and blood basophils.

TABLE 9-1. Types of Hypersensitivity Reactions

HYPERSENSITIVITY	ANTIBODY	EFFECT	EXAMPLES
Type I	IgE	Mast cells release mediators	Hay fever Anaphylaxis
Type II	IgM, IgG	Cytotoxic: Cell lysis	Goodpasture's syndrome
Type III	IgM, IgG	AG-AB complex triggers complement	Serum sickness
Type IV	None	T cells infiltrate	Poison ivy dermatitis, PPD positivity

ETIOLOGY

- Foods: Milk, egg, peanuts, shellfish.
- Drugs: β-lactam antibiotics, sulfa.
- Vaccine, immune globulin, blood products.
- Latex (gloves, Foley catheters, and endotracheal tubes).
- Insect stings, venom.

SIGNS AND SYMPTOMS

- Abrupt onset and rapid progression within 5–30 minutes.
- Generalized pruritus, **urticaria, tearing,** angioedema.
- Flushing, dizziness.
- Vomiting, abdominal cramps.
- Respiratory symptoms: Upper airway obstruction (laryngeal angioedema), bronchospasm.
- Hypotension, shock.

DIAGNOSIS

- History of exposure.
- Clinical presentation.
- **Serum tryptase** (at 1, 4, and 8 hours).
- See Figure 9-1 for National Institute of Allergy and Immunologic Disease/ Food Allergy and Anaphylaxis Network diagnostic criteria.

TREATMENT

- Airway, breathing, circulation (ABC).
- Epinephrine (1:1000–0.01 mL/kg subcutaneously). Minimum dose: 0.1 mL. Maximum dose: 0.3 mL.
- Diphenhydramine 1–2 mg/kg IV, IM, or PO q4–6h.
- Cimetidine 5–10 mg/kg IV q6h (refractory cases).
- Admit if upper airway obstruction, significant bronchospasm, blood pressure instability.

URTICARIA (HIVES)

DEFINITION

Allergic (IgE-mediated), or nonallergic (nonimmunological: physical, chemical)—mediated skin lesions.

ETIOLOGY

- Infections:
  - Viruses (influenza, enterovirus, infectious mononucleosis, hepatitis).
  - Bacteria (group A β-hemolytic streptococci).
- Medications (penicillin, cephalosporin, phenytoin, barbiturate, aspirin).
- Foods.
- Insect stings.
- Autoimmune diseases.
- Malignancies.

SIGNS AND SYMPTOMS

- Raised pale and pink pruritic areas of annular or serpiginous pattern.
- Rash is often **migratory, waxing, and waning**.

DIAGNOSIS

Clinical; no tests needed.

WARD TIP

Risk factors for severe anaphylactic reaction:
- Asthma
- β-blockade
- Adrenal insufficiency

WARD TIP

Prophylaxis:
- Avoid
- ID bracelet
- Self-injectable epinephrine (Epi-pen)

WARD TIP

Viral infections are the most common causes of urticaria in children.
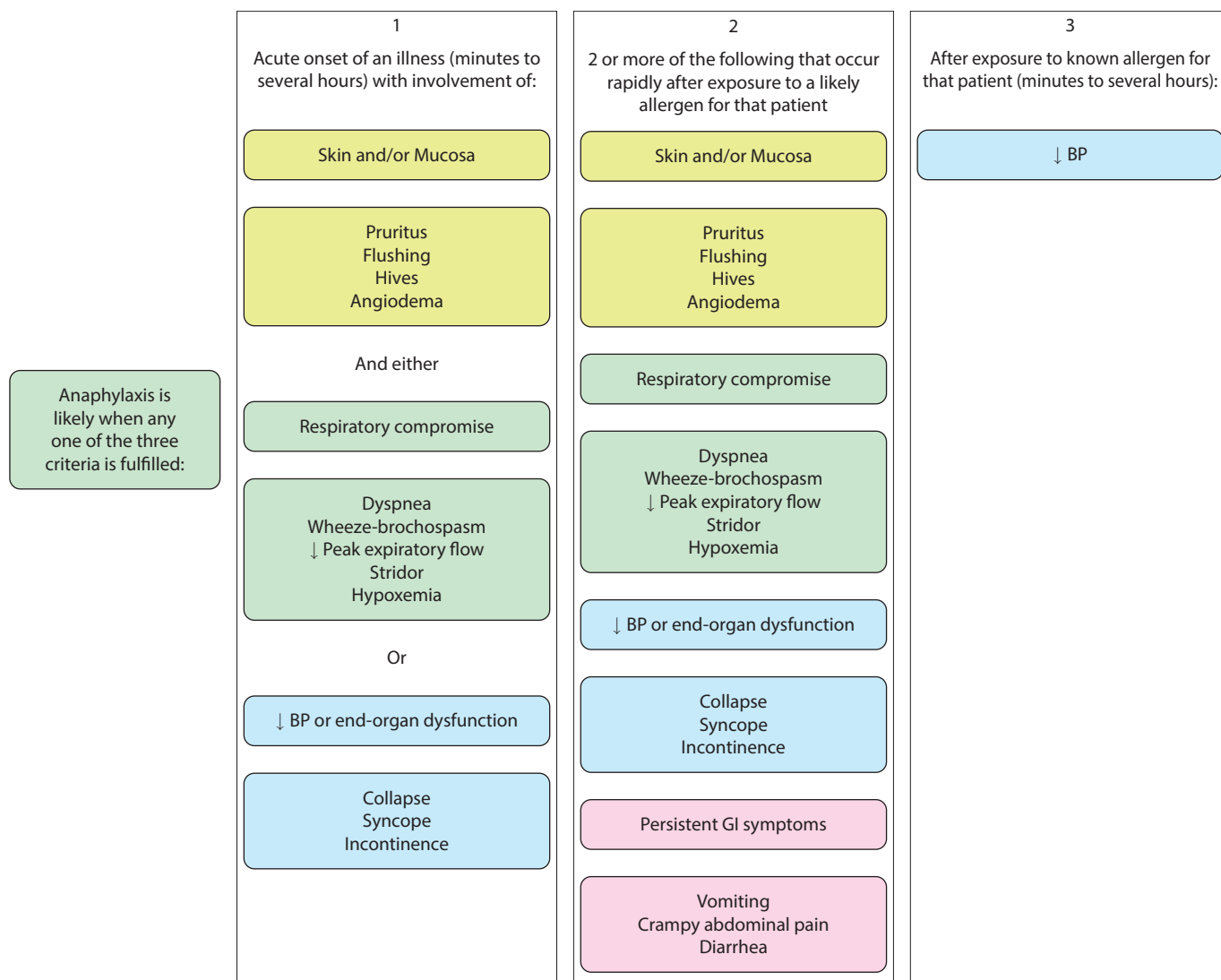
F I G U R E 9 - 1 .   **Visual representation of National Institute of Allergy and Immunologic Disease/Food Allergy and Anaphylaxis Network diagnostic criteria.** (Reproduced with permission from Manivannan V, Decker WW, Stead LG, et al. Visual representation of National Institute of Allergy and Infectious Disease and Food Allergy and Anaphylaxis Network criteria for anaphylaxis, Int J Emerg Med. 2009 Apr;2(1):3–5.)

TREATMENT

- Avoiding the precipitating cause.
- Epinephrine (1:1000 at 0.01 mg/kg) if urticaria is severe.
- Diphenhydramine.

SERUM SICKNESS

For the past 2 weeks, a 6-year-old boy has had puffy eyelids on awakening and swelling of the feet and abdomen in the afternoon. He complains of joint aches and on-and-off fever. His history includes a sting by a yellow jacket. Physical examination is significant for generalized lymphadenopathy. Urinalysis shows protein 3+ and ESR is 35. *Think: Serum sickness.*

DEFINITION

Type III hypersensitivity reaction; does not require prior sensitization.

PATHOPHYSIOLOGY

Antigen-antibody complexes form deposits in blood vessels, particularly in joints and glomeruli of the nephrons, where they activate the classical complement pathway, resulting in vasculitis.

ETIOLOGY

- Antigout medications: Allopurinol, gold salts.
- Antimicrobials: **Cefaclor,** penicillin, griseofulvin, sulfonamides.
- Antiarrhythmics: Quinidine, procainamide.
- Antihypertensives: Captopril, hydralazine.
- Thyroid medications: Thiouracil, iodides.
- Other medications: Barbiturates, phenytoin.
- Serum/blood products, anti-venoms.

SIGNS AND SYMPTOMS

- Onset 1–3 weeks after initial exposure to an offending agent.
- Fever, arthralgia, lymphadenopathy, and rash (serpiginous and urticarial or polymorphous).
- Frequent facial edema.
- **Rare** arthritis, cardiovascular and renal involvement.
- Symptoms persist 7–10 days and resolve spontaneously.

DIAGNOSIS

- Clinical.
- Low levels of C3, C4 (complement components), and CH50.

TREATMENT

Withdrawal of the offending agent.

DRUG REACTION

DEFINITION

- Abnormal immunologically mediated hypersensitivity responses.
- Relatively rare.

ETIOLOGY

Potentially any drug can cause drug reaction.

PATHOPHYSIOLOGY

- Type I (IgE mediated): Penicillin, cephalosporin.
- Type II (cytotoxic antibody mediated): Penicillin—hemolytic anemia; quinidine—thrombocytopenia.
- Type III (immune complex mediated): Penicillin, sulfonamides, cephalosporin.
- Type IV (cell mediated): Contact dermatitis—Neosporin.

CLINICAL CRITERIA

- Reactions do not resemble pharmacologic action of the drug.
- Similar to those that may occur with other allergens.
- Timing: 7–10 days.
- Reproduced by minute doses.
- Discontinuation may result in resolution.

SIGNS AND SYMPTOMS

- Mild rash to anaphylaxis.
- **Fixed drug eruptions:** Recur at the same site after each administration of causative drug (sulfonamides are the most common).

WARD TIP

Most common causes of drug reactions: penicillin, sulfonamide.

WARD TIP

Drug Reactions
- Most are afebrile.
- Eruption may worsen before improving after discontinuation of the drug.

WARD TIP

The most common site for the manifestation of drug reactions is the skin.

DIAGNOSIS

- Eosinophilia is a clue but is not diagnostic.
- Skin test is available for penicillin. It is indicated for the patients with a history of penicillin-associated anaphylaxis, urticaria, or serum sickness.
- Radioallergosorbent test (RAST).

DISPOSITION

- Discontinue likely offending agent.
- Admit if:
  - Stevens-Johnson syndrome.
  - Toxic epidermal necrolysis.
  - Severe drug reaction.
  - Respiratory distress.

PENICILLIN ALLERGY

TYPES

Wide variety of allergic reactions:
- Type I: Anaphylaxis.
- Type II: Hemolytic anemia.
- Type III: Serum sickness.

AMPICILLIN/AMOXICILLIN RASH

- Not urticaria, seen with infectious mononucleosis.
- Hyperuricemia.

FOOD ALLERGY/SENSITIVITY

PATHOPHYSIOLOGY

- Most of the true **hypersensitivities to food** products are **IgE mediated**. IgE binds to mast cells, resulting in the release of histamine and other mediators. Most common triggers are peanuts, shellfish, and eggs.
- Early presentation in life. Only ~5% of children under the age of 4 years have food hypersensitivity. It is seen even less frequently in older children.
- Most **adverse reactions** to food **do not** have an immunologic basis.
- Nonimmunologic food intolerances are common, like enzyme deficiencies (lactase deficiency, vomiting, diarrhea).

SIGNS AND SYMPTOMS

- **IgE-mediated hypersensitivity** reactions start **within minutes** of the responsible food intake, and often are associated with urticaria, edema, and anaphylaxis (see below).
- **Allergic enterocolitis of infancy** with vomiting and diarrhea (becomes bloody) represents hypersensitivity to cow's milk proteins, but is **not** IgE mediated. It → failure to thrive. Half of infants reacting to the cow's milk protein also react to soy protein. Note early presentation in the first month of life.
- **Gluten-sensitive enteropathy** is also a non-IgE-mediated food hypersensitivity (celiac disease), and also → failure to thrive. Gradual onset of symptoms in the **second half of infancy**, when the child starts to eat grains (cereal) containing gluten protein.

WARD TIP

Most common food allergies:
- Peanut
- Shellfish
- Eggs

TREATMENT

Avoidance of offending agent.

EOSINOPHILIC ESOPHAGITIS

DEFINITION

Chronic, immune-mediated or antigen-mediated esophageal disease characterized by esophageal dysfunction and eosinophil-predominant inflammation. A common cause of feeding problems in children.

DIAGNOSIS

Endoscopy with multiple biopsies.

Must rule out GERD and specific food allergy prior to diagnosis.

TREATMENT

Elimination diet based on allergen testing.

Topical glucocorticoids, e.g., swallowed fluticasone.

STEVENS-JOHNSON SYNDROME (SJS; ERYTHEMA MULTIFORME MAJOR)

DEFINITION

Extreme variant of erythema multiforme (EM) with systemic toxicity and involvement of the mucous membranes.

ETIOLOGY

- Drugs: Sulfonamides and anticonvulsants.
- *Mycoplasma pneumoniae*, herpes simplex virus.

SIGNS AND SYMPTOMS

- Prodromal phase (1–14 days): Fever, headache, malaise.
- Mucosal involvement:
  - Exudative conjunctivitis.
  - Oral erosions on the palate and gingivae.
  - Urethritis, vaginitis.
- Skin involvement: Target lesions—annular, with pink halo surrounding a pale halo and erythematous center. May have central blistering. Palms and soles are involved.
- **Nikolsky's sign:** Separation of normal epidermis at the basal layer caused by sliding finger pressure ("rubbed off" line).
- See Dermatologic Disease chapter.

DIAGNOSIS

- **Clinical criteria:** Cutaneous lesion plus at least two mucosal surfaces involved.
- Skin biopsy is not indicated (would show perivascular mononuclear cell infiltrate).

TREATMENT

- Hospitalization for supportive care.
- Intravenous (IV) hydration.
- Topical steroids and anesthetics as needed.

EXAM TIP

A 9-year-old male child presents for follow-up of dysphagia. His parents state that he has not been eating well, preferring to drink shakes and juices instead of eating meals. When he is forced to eat solid foods, the child frequently vomits within minutes. Family history is noncontributory. Physical examination is unremarkable except for low body mass. Endoscopic report shows profound esophageal eosinophilia with eosinophilic abscesses, mast cells, and inflammation. A prior trial of PPIs was unsuccessful. *Think: eosinophilic esophagitis.*

WARD TIP

Mild EM does not progress to SJS.

WARD TIP

The oral cavity is almost always involved in erythema mulitforme major.

Immunodeficiencies

- A constellation of infection types and frequencies are concerning for primary immunodeficiencies (see Table 9-2).
- Primary (congenital) immune deficiencies (PI) (Table 9-3) can be differentiated by presentation.
- PI are characterized by recurrent infections or are unusually hard to cure, if someone has two or more of the warning signs listed in the Table 9-2 he or she needs to be evaluated for a PI.

TABLE 9-2. 10 Warning Signs of Primary Immunodeficiency

1. Four or more new ear infections within 1 year
2. Two or more serious sinus infections within 1 year
3. Two or more months on antibiotics with little effect
4. Two or more pneumonias within 1 year
5. Failure of an infant to gain weight or grow normally
6. Recurrent, deep skin or organ abscesses
7. Persistent thrush in mouth or fungal infection on skin
8. Need for intravenous antibiotics to clear infections
9. Two or more deep seated infections including septicemia
10. A family history of PI

TABLE 9-3. Phagocytic and Chemotactic Disorder

DISORDER	INHERITANCE	DEFECT	CLINICAL	INFECTIONS	DIAGNOSIS
Chronic granulomatous disease	X-linked	Pyruvate deficiency in PMNs and macrophages	Gingivitis, seborrheic dermatitis, retinitis pigmentosa	Deep soft tissue abscesses, lymphadenitis, *Staphylococcus, Aspergillus*	Neutrophil oxidation test NBT = old Leukocytosis
Chédiak-Higashi	Autosomal recessive	Abnormal chemotaxis and fusion of intracellular granules	Partial albinism, progressive neuropathy, HSM	Skin and lung *Staphylococcus*	Chemotaxis test, leukopenia
Job (hyper-IgE) syndrome	Autosomal dominant	Connective tissue and chemotaxis disorder	Coarse features, eczema, lax joints	Skin and lung, *Staphylococcus, Aspergillus*	IgE > 10,000, eosinophilia
Leukocyte Adhesion Deficiency	Autosomal recessive	Impaired phagocyte recruitment from blood due to impaired adhesion	Delayed separation of umbilical cord, poor wound healing	Severe gingivitis, bacterial infections without pus	Neutrophilia, flow cytometry for CD18

HSM, hepatosplenomegaly; NBT, nitroblue tetrazolium; PMN, polymorphonuclear neutrophil.

- **Age of onset:** Neutrophil defects present in the first few months of life. Innate immunity and T-cell defects present in the first 3–4 months of life, whereas B-cell disorders present after 6 months of age, when maternal antibodies disappear.
- **X-linked inheritance:** Similar case in a male relative (Bruton's, Wiskott-Aldrich, chronic granulomatous disease [CGD]).
- **Sites of infection:**
  - Phagocytes (CGD): Sinopulmonary and soft tissues.
  - Immunoglobulin deficiencies: Sinopulmonary and gastrointestinal (*Giardia*).
  - T cells: Disseminated (mycobacteria, varicella-zoster virus).
- **Types of microorganisms**
  - Intracellular infections in T-cell disorders (viruses, mycobacteria, *Pneumocystis*).
  - Extracellular encapsulated organisms (*Streptococcus pneumoniae*, *Haemophilus influenzae* type B, and group A streptococcus) and *Giardia* in B-cell disorders.
  - Extracellular encapsulated organisms (*Streptococcus pneumoniae*, *Haemophilus influenza*) and *Neisseria* infections in late complement deficiency.
  - *Staphylococcus, Pseudomonas, Escherichia coli*, and *Aspergillus* in neutrophil disorders.
- **Associated problems**
  - Malignancies tend to accompany T-cell defects; congenital heart disease and hypocalcemia indicates DiGeorge syndrome; atopic dermatitis indicates hyper-IgE syndrome, abnormal gait and telangiectasia indicates ataxia-telangiectasia, and an easy bruising/bleeding disorder suggests Wiskott-Aldrich syndrome.
- Workup
  - Complete blood count (CBC) with differential white blood cell count and morphology, hemoglobin, and platelet count (B and T lymphocyte disorders, phagocytic disorders), quantitative immunoglobulins (B lymphocyte disorders), CH50 (complement disorders).
  - Radiograph of area of infection (chest, sinus, mastoids, or long bones).
  - Cultures, if appropriate.

CHRONIC GRANULOMATOUS DISEASE (CGD)

DEFINITION

- Most common inherited phagocyte disorder.
- 70% X-linked, 30% autosomal recessive.

PATHOPHYSIOLOGY

- Defect in NADPH oxidase complex leads to defective production of reactive oxygen species in neutrophils and macrophages.
- Susceptibility to **catalase-positive** microorganisms: *Aspergillus species, Staphylococcus aureus, Burkholderia, Serratia, Nocardia.*
- Granulomatous inflammatory responses occur due to macrophage functional impairment.

SIGNS AND SYMPTOMS

- Recurrent infections in the first year of life are usually the first symptom. Granulomatous lesions in the lungs, skin, and liver are common.
- Growth failure, abnormal wound healing, diarrhea.
- Recurrent bacterial and fungal infections: Pneumonia, abscesses of the skin, soft tissue, organs (perianal/perirectal, liver, lung), lymphadenitis,

EXAM TIP

A 10-month-old male presents with a temperature of 101.6°F (38.7°C) and a 3 × 4-cm abscess of the left buttock. His WBC count is 19.9, 77% neutrophils. At the age of 5 months he had staphylococcal cervical lymphadenitis that required drainage. His uncle also had recurrent abscesses. *Think: CGD.*

WARD TIP

Catalase-positive infections in CGD: *Aspergillus, S. aureus, Burkholderia, Serratia, Nocardia.*

osteomyelitis, bacteremia/fungemia, superficial skin infections (cellulitis/impetigo).

- Hepatomegaly, splenomegaly, lymphadenopathy (enlarged by granulomas).

DIAGNOSIS

- Hypergammaglobulinemia.
- Dihydrorhodamine oxidation test (more sensitive) or Nitroblue tetrazolium test.
- Genetic testing confirms diagnosis.

TREATMENT

- Antimicrobial prophylaxis with TMP-SMX, itraconazole, and interferon-gamma.
- Aggressive, early treatment of infection.
- Surgical excision of abscesses.
- Hematopoietic cell transplantation effective for refractory infection.

CHÉDIAK-HIGASHI SYNDROME

DEFINITION

Autosomal-recessive syndrome caused by mutations of the lysosomal trafficking regulator gene, resulting in abnormal chemotaxis and fusion of intracellular granules.

SIGNS AND SYMPTOMS

- Recurrent skin infections and pneumonias (*Staphylococcus aureus*).
- Partial oculocutaneous albinism.
- Progressive peripheral neuropathy.

DIAGNOSIS

- Giant gray granules in the cytoplasm of nucleated cells.
- Leukopenia, neutropenia.
- Chemotaxis test.

TREATMENT

- Ascorbic acid has no effect.
- Antibiotics for acute infections.
- **Bone marrow transplantation** (does not prevent or cure peripheral neuropathy).

JOB SYNDROME (HYPER-IGE)

DEFINITION

- Autosomal dominant neutrophil chemotactic disorder caused by JAK-STAT signaling pathway defect (STAT3 gene mutation).
- Hyperimmunoglobulinemia E with impaired chemotaxis.
- *Characteristic findings include* eczema, recurrent "cold," staphylococcal skin abscesses, sinusitis, and otitis media.

SIGNS AND SYMPTOMS

- Recurrent staphylococcal infections.
- Eczema.
- Lax (hyper-extensible) joints.
- Scoliosis, coarse facial features, retention of baby teeth.

EXAM TIP

A 10-year-old boy has a history of severe pneumonia with empyema at the age of 5 years. He is also allergic to pollens and animal dander. Now he has fever of 102.3°F (39.1°C). On examination, coarse facial features, eczematous patches on the extremities, and a tender 4 × 3-cm right anterior cervical lymphatic node are present. WBC is 24.7. *Think: Job syndrome.*

EXAM TIP

Job syndrome:
- Eczema
- Eosinophilia
- Lax joints
- Staph infections

DIAGNOSIS

- IgE >10,000 IU/mL.
- Eosinophilia.

TREATMENT

- Skin hydration and management of pruritus.
- TMP-SMX prophylaxis for patients with frequent infections.
- Omalizumab (monoclonal anti-IgE antibody)—inadequately tested therapy.
- Hematopoietic cell transplant.

LEUKOCYTE ADHESION DEFICIENCY (LAD)

DEFINITION

LAD type 1 is an autosomal recessive defect in the integrin CD18, which impairs tight adhesion of neutrophils to endothelium. LAD type 2 is a metabolic defect that impairs leukocyte ability to bind selectins and roll along the endothelium.

SIGNS AND SYMPTOMS

- Failure of separation of umbilical cord, with secondary omphalitis and sepsis.
- Poor wound healing.
- Bacterial infections without pus.
- Severe gingivitis.
- The absence of pus at sites of infection is a striking feature of neutrophil migration disorders, which prevent phagocytes from extravasating out of blood vessels to sites of infection in the tissue. Death usually occurs in childhood secondary to sepsis if left untreated.

DIAGNOSIS

- Neutrophilia in the absence of infection; during infection, count can range >50,000.
- Tissue biopsies.
- Flow cytometry testing for CD18.

TREATMENT

- Oral hygiene.
- Aggressive antibiotic management of infections.
- Hematopoietic cell transplant for severe cases.

COMPLEMENT DEFICIENCY

Deficiency of complement proteins leads to severe immunodeficiency; different deficiencies are associated with specific infections as noted below.

COMPLEMENT

Complex system of nine serum proteins (C1–C9).

FUNCTIONS OF COMPLEMENT

- Opsonization.
- Bacteria cell lysis.
- Facilitating chemotaxis.

ASSOCIATED DISEASES

- C1q deficiency: Systemic lupus erythematosus (SLE).
- C1 esterase inhibitor (C1 INH) deficiency: Hereditary angioedema.

> **EXAM TIP**
>
> A 2-month old male presents with fever. On physical examination, his temperature is 103°F, HR 200 beats/min, RR 50 breaths/min, and appears lethargic. He has not had separation of his umbilical cord, which remains attached, and the surrounding skin is erythematous and indurated. The patient is admitted with diagnosis of sepsis and labs are obtained. Her white blood cell count is 22,000/mm³ with 90% neutrophils. *Think: defective neutrophil migration.*

> **EXAM TIP**
>
> A 16-year-old female presents with a second episode of meningococcal meningitis. Her CH50 is 78%. *Think: C5–C9 deficiency.*

> **EXAM TIP**
>
> Hypocomplementemia occurs in patients with lupus nephritis and poststreptococcal glomerulonephritis, but not in Henoch-Schönlein purpura or minimal change disease.

TABLE 9-4. **Complement Deficiencies**

Deficiency	Mechanism	Infections	CH50
C2 (most common)	↓ opsonins	Pyogenic in one-fifth	<10%
Properdin (X-linked)	↓ opsonins	Pyogenic	Normal (AH50 low)
C5–C9	↓ membrane attack	Recurrent *Neisseria meningitidis*	>50%

- C2 deficiency: Pneumococcal infections.
- C5–C9 terminal complement deficiency: *Neisseria* infection (Table 9-4).

DIAGNOSIS

- CH50 screening test.
- Hereditary angioedema: Laryngeal edema (airway obstruction); intestinal edema (colicky abdominal pain); edema of face, limbs, and genitals. Bradykinin-mediated.
- Combined B- and T-cell disorders.

SEVERE COMBINED IMMUNODEFICIENCY (SCID)

A 4-month-old female just diagnosed with failure to thrive (FTT) presents with respiratory distress. On physical examination, she has a temperature of 101°F (38.3°C), RR 70 breaths/min, and oxygen saturation 91% (on room air). Oral thrush and bilateral rhonchi were present. There is no lymphadenopathy. Her white blood cell count is 16.2, 83% neutrophils, 11% monocytes. Chest x-ray shows diffuse bilateral interstitial infiltrates. *Think: PCP.*
Infection with opportunistic organisms such as PCP is common in infants with SCID. Absence of lymph nodes in an infant with FTT in the first few months of life is suggestive of SCID. Oral thrush, extensive diaper rash, and failure to thrive are the prominent features.

DEFINITION

Abnormalities of both humoral and cellular immunity.

ETIOLOGY

- A group of genetic abnormalities that result in severe T-cell depletion (or dysfunction) and B-cell dysfunction (e.g., enzyme deficiencies → defect in stem cell maturation).
- **Adenosine deaminase (ADA) deficiency:** One-third of all SCID cases.

SIGNS AND SYMPTOMS

- Presents within first 3 months with diarrhea, pneumonia, otitis, sepsis, FTT, and skin rashes.
- Frequency and severity of infections.
- Persistent infection with **opportunistic organisms** (*Candida*, mycobacteria, herpes viruses, CMV, PCP).
- Absent lymphatic nodes, hypoplastic thymus.

DIAGNOSIS

- Lymphopenia: ALC (absolute lymphocyte count) <500.
- ↓ serum IgG, IgA, and IgM.

- Low or no T and B cells.
- SCID is screened for on newborn screen in 32 states.

TREATMENT

- Aggressive antimicrobial treatment of even mild infections.
- Palivizumab for RSV prophylaxis during appropriate season.
- Recombinant ADA for replacement therapy.
- IVIG.
- Hematopoietic cell transplantation (HCT).

PROGNOSIS

Death within first year if untreated.

HYPER-IGM SYNDROME

DEFINITION

- X-linked defect in CD40 ligand, leading to impaired T-cell "help" to B cells.
- Characterized by failure of isotype switching from IgM to IgA, IgG, and IgE.

SIGNS AND SYMPTOMS

- Recurrent infections with pyogenic bacteria due to reduced opsonizing IgG antibodies.
- Presentation after first 6 months of life.
- Severe intracellular infections due to impaired cellular immunity (*Pneumocystis jirovecii*).
- Malignancies.

DIAGNOSIS

- Serum Ig analysis: Markedly high IgM, low IgG, no IgA and IgE.

TREATMENT

- IVIG.
- High mortality rate.

T-CELL DISORDERS

Langerhans Cell Histiocytosis (LCH)

> An 18-month-old female presents with two "bumps on the head." Physical examination shows weight below 3rd percentile; two palpable masses on the scalp; and scaly, greasy patches of rash over the scalp, eyebrows, neck, and in the ear canals; generalized lymphadenopathy; and hepatosplenomegaly. WBC: 5.6, Hb 8.4, platelet count 76. Lateral skull radiograph shows two well-defined lytic lesions. *Think: Langerhans cell histiocytosis.*
>
> Patients with this disease typically present with a scaly seborrhea and eczematous rash that involves the scalp, ear canals, abdomen, and intertriginous areas of the neck and face. Typical age of presentation is under 2 years. There is a potential for pancytopenia because of hematopoietic involvement.

DEFINITION

- Previously known as *Letterer-Siwe disease*.
- CD207+ cell proliferation in multiple tissues triggering granulomatous inflammation.
- Manifestation of immune dysregulation that is incompletely understood.

SIGNS AND SYMPTOMS

- Skeleton involved (80%): Skull, vertebrae (eosinophilic granuloma, lytic lesions).
- Skin (50%): Seborrheic or eczematoid dermatitis in a child of <2 years of age.
- Lymphadenopathy (33%).
- Hepatosplenomegaly (20%).
- Anorexia, FTT.
- Exophthalmos.
- Pituitary dysfunction: Growth retardation, diabetes insipidus.
- Systemic manifestations: Fever, weight loss, irritability, FTT.
- Bone marrow suppression: Anemia, thrombocytopenia, neutropenia.

LAB

- Complete blood count (CBC), liver function tests (LFTs), coagulation profile.
- Chest x-ray.
- Skeletal survey.
- Urine osmolality.
- Tissue biopsy of any skin or bone lesions.

TREATMENT

- Treatment directed at arresting the progression of lesion (low-dose local radiation).
- Prednisolone and vinblastine combination therapy.
- Spontaneous remission.

DIGEORGE SYNDROME

A 2-month-old infant with congenital heart disease and cleft palate is hospitalized with cough and tachypnea. He has a history of a seizure episode. Chest x-ray shows diffuse infiltrates and no thymic shadow. Serum calcium is 6.5 mg/dL. *Think: DiGeorge syndrome.*

DiGeorge syndrome is a T-cell deficiency that results from failure of development of the third and fourth pharyngeal pouches, which are responsible for the development of thymus and parathyroid glands. These result in lack of T-cell-mediated immunity, tetany, and congenital defects of the heart and great vessels. It is important to recognize this diagnosis because without treatment it is fatal.

PATHOPHYSIOLOGY

- Deletion in chromosome 22, resulting in a defect of development of the third and fourth pharyngeal pouches.
- Phenotypical translation into midline defects of the heart, head, parathyroids, and thymus.

SIGNS AND SYMPTOMS

- Dysmorphic features: Hypertelorism, cleft palate.
- Congenital heart disease: **Truncus arteriosus, interrupted aortic arch**.
- Hypoparathyroidism presents as hypocalcemic seizures (**"tetany"**).
- Recurrent infections: depending on T-lymphocyte counts. Opportunistic infections (OIs) in severe cases.

DIAGNOSIS

- Calcium level and parathyroid hormone.
- T-cell count (variable).
- Chest x-ray: No thymic shadow.

- Echocardiogram.
- **Fluorescent in-situ hybridization (FiSH)** test detects the 22q11.2 deletion.

TREATMENT

- Evaluate for hearing difficulties.
- Cultured thymic transplant, if ALC <100.
- HCT provides improved immune function, but carries severe risk of graft-versus-host disease (GVHD) unless donor is HLA-identical.
- Use **irradiated blood products** only.

ATAXIA-TELANGIECTASIA (AT)

DEFINITION

Autosomal-recessive disorder of DNA repair that presents as telangiectasias, ataxia, and variable extent of T-cell deficiency, with progressive loss of T helpers. Both humoral and cellular immunodeficiency.

SIGNS AND SYMPTOMS

- Usually presents during first 6 years, wheelchair confinement by 10–12 years.
- **Earliest sign: Telangiectasias on the sclerae** (misdiagnosed as "pink eye").
- Progressive cerebellar ataxia.
- Chronic sinusitis, bronchiectases.
- OIs.
- ↑ risk of malignancy (lymphomas, leukemia).

LAB

- Absence of antibodies after vaccination.
- Low IgA and IgM.
- T4 lymphocytes decline over time.
- ↑ serum α-fetoprotein.

TREATMENT

- Supportive therapy.
- Improve pulmonary function.
- Prophylaxis of OIs.
- Avoidance of ionizing radiation.
- Twenty-three valent pneumococcal vaccine every 10 years.

CHRONIC MUCOCUTANEOUS CANDIDIASIS (CMC)

DEFINITION

- T-cell dysfunction: Inability to recognize candidal antigens.
- A heterogeneous group of disorders characterized by recurrent or persistent superficial candidal infections of the skin, nails, and mucous membranes.

SIGNS AND SYMPTOMS

- Refractory thrush may extend to the esophagus.
- Refractory severe diaper rash.
- Angular cheilitis.
- Nails thickened, significant edema and erythema of the surrounding peri-ungual tissue.
- Often associated with endocrinopathy: Hypo/hyperthyroidism, polyendo-crinopathy.

> **EXAM TIP**
>
> Ataxia-telangiectasia:
> - Telangiectasias of conjunctivae and exposed areas
> - Ataxia
> - Lymphoma

> **WARD TIP**
>
> Thymic hypo- or aplasia results in a deficiency of functional T cells.

TREATMENT

- Systemic antifungals.
- Skin care.

WISKOTT-ALDRICH SYNDROME

> A 10-month-old boy presents with oral thrush despite 10 days of treatment with nystatin. He had four episodes of otitis media. Physical examination shows oral thrush and multiple patches of eczema. Both tympanic membranes are dull. CBC shows the following: WBC 7.6, Hb 11.3, platelet count 97. His uncle died in infancy of infection. *Think: Wiskott-Aldrich syndrome.*
>
> Wiskott-Aldrich syndrome is an X-linked recessive syndrome characterized by the triad of eczema, thrombocytopenia, and immunodeficiency. The initial manifestation usually is petechiae or bleeding in the first few months of life. Classic presentation is thrombocytopenia, eczema, and recurrent otitis media.

DEFINITION

X-linked-recessive disorder of cell cytoskeleton, presenting as eczema, thrombocytopenia, and ↑ susceptibility to infection.

SIGNS AND SYMPTOMS

- Atopic dermatitis/eczema (see Table 9-5).
- Thrombocytopenic purpura, mucosal bleeding, bloody diarrhea, cerebral hemorrhage.

> **EXAM TIP**
>
> Wiskott-Aldrich syndrome:
> - Eczema
> - Thrombocytopenia
> - ↑ IgA/IgE

TABLE 9-5. Combined and Primary T-Cell Immune Deficiencies

DISORDER	DEFECT	LYMPHOCYTES	IMMUNOGLOBULINS	CLINICAL	INFECTIONS	TREATMENT
SCID group (ADA = one third)	Variable enzyme deficiencies	Low/no T, some/no B	Low/no titers	0–3 months FTT, thrush, ALC < 500	PCP, sepsis, severe VZV	BMT, ADA replacement
DiGeorge	Point mutation Midline defects No thymus	Low/no T	Low/no titers	Low Ca, truncus arteriosus	Same	Thymus transplant (ALC < 100)
Wiskott-Aldrich	X-linked, defective cytoskeleton of the cells	Normal #	High IgA, IgE Low IgM, titers	Eczema, TCP	OIs (PCP), severe HSV and VZV	BMT
Ataxia-telangiectasia	AR, defect in DNA repair	Progressive loss of T4	Low IgA, IgM, and titers	Wobbly gait, red sclerae, lymphomas	OIs, sinopulmonary	Antibiotics
Chronic mucocutaneous candidiasis	T cells don't respond to candidal antigens	Normal #	Normal	Endocrinopathy (thyroid)	Persistent thrush, thickened nails	Systemic antifungal

ADA, adenosine deaminase; ALC, absolute lymphocyte count; AR, autosomal recessive; BMT, bone marrow transplantation; FTT, failure to thrive; HSV, herpes simplex virus; OIs, opportunistic infections; PCP, *Pneumocystis jirovecii* pneumonia; SCID, severe combined immunodeficiency; TCP, thrombocytopenia; VZV, varicella-zoster virus.

- Recurrent infections in infancy: Pneumococcal (otitis, pneumonia), persistent thrush.
- OIs: *Pneumocystis jirovecii* pneumonia (PCP).

LABS

- ↓ IgM.
- ↑ IgA and IgE.
- Absence of antibodies after vaccination.

TREATMENT

- TMP-SMX prophylaxis for PCP and acyclovir prophylaxis for recurrent HSV.
- IVIG in patients with severe antibody deficiency.
- Rituximab (monoclonal antibody directed against the CD20 B-cell antigen) for autoimmune cytopenias.
- Elective splenectomy may be used for thrombocytopenia and bleeding, but increases risk for sepsis.
- HCT.
- Gene therapy.

COMMON VARIABLE IMMUNODEFICIENCY (CVID)

DEFINITION

- A group of disorders of T- and B-cell interaction and cytokine production, resulting in impaired IgM to IgG switch and in the absence of protective antibody titers (see Table 9-6).
- Often (one fourth) familial.
- Involves the formation of autoantibodies.

SIGNS AND SYMPTOMS

- Two peak ages of onset: Children aged 1–5 years and 16–20 years old.
- Lymphadenopathy, splenomegaly.
- Association with autoimmune diseases: Inflammatory bowel disease (IBD), sprue-like syndrome, arthritis.

TABLE 9-6. B-Cell Disorders and Immunoglobulin Deficiencies

DISORDER	DEFECT	LYMPHOCYTES	IMMUNOGLOBULINS	CLINICAL	INFECTIONS	TREATMENT
Bruton's agamma-globulinemia	X-linked arrest of B-cell maturation	No B Normal T	Low/no titers	No tonsils, no palpable lymph nodes	Pneumococcal Rotaviral *Giardia*	IVIG
Selective IgA deficiency	No switch to IgA	Normal #	No IgA Normal IgM, IgG, and titers	Allergies, arthritis, IBD	Mostly respiratory	IVIG is contraindicated
CVID (a group of disorders)	Abnormal T- and B-cell interactions One-fourth familial	Normal #	Normal IgM Low IgA, IgG, and titers	Lymphadenopathy, autoimmune lymphomas	Pneumococcal, *Giardia*, sinusitis	IVIG if IgG <400

CVID, common variable immunodeficiency; IBD, inflammatory bowel disease; IVIG, intravenous immunoglobulin.

- Lymphoid interstitial pneumonitis, granulomas on various organs.
- ↑ risk of malignancies: Non-Hodgkin lymphoma, gastric carcinoma.
- Sinopulmonary infections: Pneumococcal, *Mycoplasma*.
- Gastrointestinal (GI) infections: *Giardia*.
  - Usually a diagnosis of exclusion
  - Patients with CVID have normal numbers of B-lymphocytes which can help differentiate from patients with X-linked agammaglobulinemia and autosomal recessive agammaglobulinemia.

BRUTON'S X-LINKED AGAMMAGLOBULINEMIA

DEFINITION

- X-linked tyrosine kinase deficiency resulting in the arrest of B-cell maturation at pre-B cell stage. Gene defect in Xq22 (see Table 9-7).
- Severe hypogammaglobulinemia.

SIGNS AND SYMPTOMS

- No tonsils.
- No palpable lymphatic nodes.
- Recurrent/chronic sinopulmonary infections with encapsulated organisms (*Haemophilus influenzae*, *Streptococcus pneumoniae*).
- Severe/chronic gastrointestinal infections due to lack of IgA *(Giardia, Salmonella)*.
- ↑ susceptibility to enteroviral meningoencephalitis.

DIAGNOSIS

Very low or absent mature B lymphocytes and all classes of immunoglobulins. No production of protective antibodies (negative titers). Genetic testing available for B-cell-specific tyrosine kinase gene mutation.

TABLE 9-7. Immunoglobulin Disorders

DISORDER	B CELLS	IgM	IgG	IgA	IgE
Hyper-IgE (Job) Syndrome	Normal	Normal	Normal	Normal	↑
Selective IgA Deficiency	Normal	Normal	Normal	↓	Normal
Transient Hypoimmunoglobulinemia of infancy	Normal	Normal	↓	Normal	Normal
Wiskott-Aldrich	Normal	↓	↓	↑	↑
Hyper-IgM Syndrome	Normal	↑	↓	↓	↓
Common Variable Immunodeficiency	Normal	↓	↓	↓	↓
Bruton's X-Linked Agammaglobulinemia	↓	↓	↓	↓	↓
Severe Combined Immunodeficiency	↓	↓	↓	↓	↓

TREATMENT

Monthly intravenous immunoglobulin.

Prophylactic antibiotics if immunoglobulin treatment alone fails.

Live vaccines are contraindicated and other vaccines do not stimulate appreciable antibody titers.

SELECTIVE IGA DEFICIENCY

DEFINITION

Deficiency of IgA-predominant immunoglobulin on mucosal surfaces due to failure of B cells to differentiate into IgA-secreting plasma cells.

EPIDEMIOLOGY

Most common of the primary antibody deficiencies: 1:700 persons.

SIGNS AND SYMPTOMS

- Usually asymptomatic; secretory IgM production increases in IgA-deficient patients.
- Allergies.
- Associated with autoimmune diseases: celiac disease, inflammatory bowel disease, SLE.

DIAGNOSIS

- IgA <5 mg/dL.
- Normal levels of other immunoglobulins and normal response to vaccination.
- Normal cell-mediated immunity.

ASPLENIA

A 7-year-old African-American girl who just immigrated from Togo presents with fever of 104°F (40°C). Physical examination did not reveal any source of fever. There is no palpable spleen. Her WBC count is 28.2, Hct 27.1, and there are Howell-Jolly bodies in RBCs. Blood culture grew *Streptococcus pneumoniae. Think: Sickle cell disease.*
Patients with asplenia are at increased risk for the development of sepsis, most commonly due to *S. pneumoniae.* Patients with sickle cell disease develop functional asplenia. Howell-Jolly bodies indicate hyposplenism.

DEFINITION

Absence of the functional spleen.

ETIOLOGY

- Congenital asplenia is suspected when an infant is born with abnormalities of abdominal viscera and complex cyanotic congenital heart disease.
- Functional asplenia may be secondary to **sickle cell disease** (SCD) or other hemoglobinopathies.
- Hyposplenia may be secondary to SLE, rheumatoid arthritis (RA), IBD, GVHD, nephrotic syndrome, or prematurity.
- Splenectomy due to trauma, Hodgkin's lymphoma, chronic ITP, and hereditary spherocytosis.

WARD TIP

Immunoglobulin infusions confer passive immunity.

WARD TIP

Infants with Bruton's agammaglobulinemia remain well for the first 6 months due to the presence of maternal IgG antibodies.

WARD TIP

Patients with selective IgA deficiency can develop anti-IgA antibodies with blood product exposure → fatal anaphylaxis with blood or IVIG infusion. **IVIG is contraindicated.**

WARD TIP

IgA is the major immunoglobulin within the upper airway.

EXAM TIP

Asplenia:
- Howell-Jolly bodies
- Encapsulated organism

WARD TIP

Children with sickle cell anemia develop functional asplenia during the first year of life, and overwhelming sepsis is the leading cause of early death in the disease.

DIAGNOSIS

- ↓ IgM antibodies, alternate complement pathway, and tuftsin.
- ↑ requirement for opsonic antibodies.
- **Howell-Jolly bodies** in erythrocytes.

COMPLICATIONS

Sepsis with encapsulated organisms:
- 0–6 months: Gram-negative enteric (*Klebsiella, Escherichia coli*).
- >6 months of age: *S. pneumoniae, Haemophilus influenzae* type B. Malaria and babesiosis are more severe.

TREATMENT

- Penicillin prophylaxis.
- Pneumococcal immunization 23 valent and 13 valent, also *H. influenzae* and meningococcal (vaccinations against encapsulated organisms).

GRAFT-VERSUS-HOST DISEASE (GVHD)

DEFINITION

- Donor lymphocytes detect host as foreign.
- Complication of BMT.

ETIOLOGY

Engraftment by immunocompetent donor lymphocytes in an immunologically compromised host.

PATHOPHYSIOLOGY

Donor T-cell activation by antibodies against host major histocompatibility complex antigens.

SIGNS AND SYMPTOMS

- **Acute: <100 days:**
    - Erythroderma.
    - Cholestatic hepatitis—abnormal LFTs.
    - Enteritis—diarrhea and cramps.
    - ↑ susceptibility to infections.
- **Chronic: >100 days:**
    - **Either:**
        - Generalized skin involvement, **or**
        - Localized skin involvement and/or hepatic dysfunction **and** liver histologic evidence of chronic aggressive hepatitis, bridging necrosis, or cirrhosis.
    - **Or:**
        - Involvement of the eye ("keratoconjunctivitis sicca" = dry eye).
        - Involvement of minor salivary glands or oral mucosa (dryness).
        - Involvement of any other target organ.

TREATMENT

- High-dose glucocorticoids.
- Immunosuppressive therapy.

WARD TIP

Requirements for the diagnosis of graft-versus-host disease:
- Graft must contain immunocompetent cells.
- Host must be immunocompromised.
- Histocompatibility differences must exist.

Infectious Disease

Occult Bacteremia

DEFINITION

Fever **without an obvious source** of infection (except otitis media) in a well-appearing child with a positive blood culture for a bacterial pathogen.

ETIOLOGY

Neonates
- Group B streptococci.
- *Escherichia coli.*
- *Listeria monocytogenes.*
- *Staphylococcus aureus.*
- Coagulase-negative *Staphylococcus* (preterm infants, catheter-related).

Children
- *Streptococcus pneumoniae* (most common).
- *Neisseria meningitidis.*
- *Salmonella typhimurium.*
- *S. aureus.*
- Group A streptococci.

SIGNS AND SYMPTOMS

- Fever >38°C (100.4°F).
- Leukocytosis—WBC often elevated, but not a reliable indicator of infection (neither sensitive nor specific).

PREDISPOSING FACTORS

- Loss of external defenses (burns, ulceration, indwelling catheter).
- Inadequate immune function.
- Nonimmunized or underimmunized.
- Impaired reticuloendothelial function (asplenia, underlying condition like sickle cell disease).

DIAGNOSTIC WORKUP

- Blood and urine cultures.
- Complete blood count (CBC): Normal WBC count is 5000–15,000 cells/L.
- Lumbar puncture if <60 days old.

TREATMENT

- Treat with antibiotics to prevent seeding of focal site (osteomyelitis, pneumonia, meningitis) or progression to septicemia.
- See Table 10-1 for age-based management criteria.

Urinary Tract Infection

DEFINITION

Growth of a single pathogen in the urine of >100,000 colony forming units (CFU)/mL in a clean catch specimen or >50,000 CFU/mL in catheterized urine samples.

WARD TIP

Group B strep is the most common cause of neonatal bacteremia and sepsis.

WARD TIP

Occult bacteremia has become very rare in the fully immunized, well-appearing child over 3 months of age. Authorities do not recommend routine blood work in well appearing, immunocompetent, immunized children just on the basis of fever.

WARD TIP

A 3-week-old male infant presents with fever, vomiting, and ↓ fluid intake. A UA reveals 100 WBCs. *Think: E. coli UTI. Next step—urine culture.*

Neonates with UTI are more likely to develop nonspecific symptoms, such as irritability, fever, and vomiting. *E. coli* is the most common organism in children of all ages. Urinalysis may show positive urinary leukocyte esterase, positive urinary nitrite, pyuria, and/or bacteruria,

T A B L E   1 0 - 1 .   Age-Based Management of Possible Occult Bacteremia in a Low-Risk Infant—Full Term, Previously Healthy, with Negative Laboratory Screen (Normal WBC Count and Urinalysis)

AGE	MANAGEMENT
<60 days	■ All considered for hospitalization and parenteral antibiotics. ■ Ampicillin and gentamicin for newborns. ■ Ampicillin + cefotaxime for second month of life.
61–90 days	■ Manage as outpatient if good follow-up, with or without one dose of ceftriaxone. ■ Unreliable follow-up: CSF exam prior to ampicillin + cefotaxime.
3–36 months	■ If fever > 102.2°F (39°C): Get WBC; cultures of blood, urine. ■ Ceftriaxone is optional if nonseptic appearance; follow-up extremely important.

CSF, cerebrospinal fluid; WBC, white blood cell count.

ETIOLOGY

Most common organisms:
- *Escherichia coli.*
- *Klebsiella.*
- *Poteus.*
- *Enterobacter.*
- *Staphylococcus saprophyticus.*
- *Enterococcus.*

SIGNS AND SYMPTOMS

- Fever >38°C (100.4°F) without a source in females under 2 years, circumcised males under 6 months, and uncircumcised males under 1 year.
- Dysuria or frequency in older children.
- Pyuria.

PREDISPOSING FACTORS

- Age—boys younger than 1 year and girls younger than 2 years. Female infants are at four times higher risk than males.
- Lack of circumcision.
- White children have a two to four times higher rate than do black children.
- GU abnormalities—structural or functional (neurogenic bladder or vesicoureteral reflux.

DIAGNOSTIC WORKUP

- Urinalysis demonstrating leukocyte esterase (more sensitive) or nitrites (more specific).
- Pyuria on microscopic evaluation (>10 wbc/hpf).
- Urine culture.
- Renal ultrasound should be performed on all first time UTIs in childhood and infancy to evaluate for hydronephrosis.
- Vesiculocystourethrogram should be performed on all patients with an abnormal ultrasound. Reflux of urine increases risk of renal scarring.

> **WARD TIP**
>
> Urinary tract infections are the most common occult serious bacterial illness in infants and young children.

> **WARD TIP**
>
> Occult bacteremia has become very rare in the fully immunized, well-appearing child over 3 months of age. Authorities do not recommend routine blood work in well-appearing, immunocompetent, immunized children just on the basis of fever.

TREATMENT

- Empiric treatment with antibiotics should begin as soon as diagnosis is made. Cephalosporins are a good first-line agent.
- Hospitalize infants under 2 months and all ill appearing.

Sepsis

DEFINITION

- A systemic inflammatory response to infection that results in hemodynamic and metabolic compromise.
- Hypoperfusion abnormalities in sepsis result in lactic acidosis, oliguria, altered mental status, and an ↑ oxygen utilization (oxygen dissociation curve moves to right).

DIAGNOSTIC CRITERIA

Manifested by ≥2 conditions:
- Hyper- or hypothermia (≥101.3°F [38.4°C] or <96.8°F [36°C]).
- Tachycardia (age-based elevation: infants >180, preschool aged >160, school aged >150).
- Tachypnea (respiratory rate: infant >60, child >50).
- WBC count >15,000 or <5000 cells/L and bandemia is common but not necessary for diagnosis.

ETIOLOGY

Same as for bacteremia above.

SIGNS AND SYMPTOMS

- May be nonspecific and include ill-appearance, listlesslessness, hyperthermia or hypothermia.
- Vomiting and poor feeding are common, nonspecific findings in **any infant** with fever.

DIAGNOSIS

- Presumed infection with systemic inflammatory response leading to compromised perfusion states. Sepsis is a clinical condition and can be caused by viral as well as bacterial causes.
- Ten percent will have negative blood cultures.

RISK FACTORS

- Age (younger children at greater risk).
- Prematurity.
- Immunodeficiency (may be underlying condition or medication related—i.e., steroids).
- Indwelling catheters.
- Contact with known N. *meningitidis* or *Haemophilus influenzae* infection.

A 3-month-old female is brought to the ED with fever, vomiting × 1, ↓ activity, and poor breast-feeding for 1 day. Previous history is unremarkable. Physical examination shows an ill-appearing girl with a temperature of 101.1°F (38.4°C), HR 196 beats/min, and no identifiable focus of infection. *Think: Sepsis.*

Young infants are at increased risk for serious infection. They may present with nonspecific signs and symptoms and often lack focal signs of infection.

SEPTIC SHOCK

DEFINITION

Clinical evidence of infection plus persistent hypotension despite adequate fluid resuscitation, along with evidence of hypoperfusion abnormalities or end organ dysfunction.

DIAGNOSTIC CRITERIA

Meet sepsis criteria, **plus** one of the following:
- Hypoperfusion requiring >40 mL/kg isotonic fluid (crystalloid or colloid) and/or inotropic support.
- Hypotension (age-based).
- More than one manifestation of organ hypoperfusion. (e.g., oliguria, elevated hepatic enzymes, altered mental status, prolonged capillary refill).

TREATMENT

- IV broad-spectrum antibiotics.
- Manage shock with aggressive IV fluid resuscitation and vasopressors as needed to maintain blood pressure, perfusion, and oxygenation.

MENINGOCOCCEMIA (FIGURE 10-1)

A 5-year-old boy presents with sudden onset of chills, fever, and listlessness. Physical examination shows a temperature of 103.5°F (39.7°C) and palpable, reddish-purple, nonblanching spots (purpura). He is rapidly progressing to shock. *Think: Meningococcemia.*

Typical presentation is sudden onset of fever, vomiting, headache, and lethargy. Most patients have petechiae on presentation. The infection can progress rapidly to profound shock and DIC.

- Presents nonspecifically with petechiae, then purpura, and finally eschar (skin breakdown in areas of profound hypoperfusion).

WARD TIP

Rule of thumb for hypotension: lowest acceptable systolic blood pressure is 70 + 2× (age in years).

EXAM TIP

Meningococcemia
- Fever
- Purpura
- Rapid progression to shock

F I G U R E 1 0 - 1 . Meningococcemia. (Reproduced, with permission, from Knoop KJ, Stack LB, Storrow AB, et al. *Atlas of Emergency Medicine*, 3rd ed. New York, NY: McGraw-Hill, 2010: 423. Photo contributor: Richard Strait, MD.)

- Typical rash distribution: Buttocks and lower extremities.
- Progresses rapidly (within hours) to septic shock due to endotoxin.
- Establish diagnosis by culture of blood, cerebrospinal fluid (CSF), and skin lesions.
- Adrenal hemorrhage (Waterhouse-Friedrichsen syndrome) and insufficiency are classic complications.

TREATMENT

- IV ceftriaxone or cefotaxime is treatment of choice until sensitivities are available.
- See Septic Shock Treatment—think fluid resuscitation and vasopressor support.

Fever and Rash (see Table 10.2)

- **Enanthem:** Lesion on mucosal surface (mouth).
- **Exanthem:** Lesion on the skin (rash).
- **Polymorphous rash:** Consists of various primary elements.
- Primary elements of rash (see Dermatologic Disease chapter for specifics of rashes):
  - Macule: Flat, discolored, blanching spot.
  - Papule: Small, raised spot.
  - Vesicle: Small, round fluid-filled lesion.
  - Pustule: Small, round pus-filled lesion.
  - Petechia: **Pinpoint** nonblanching purplish spot (extravasation).
  - Purpura: Small, raised, purplish nonblanching lesion (extravasation).
  - Erythroderma: Confluent redness of the skin.
  - Excoriation: Crust.
  - Eschar: Dead tissue (or ulcer) covered by dry, dark scab.
- **In order to recognize infection, keep in mind:**
  - Primary element(s) of rash.
  - Distribution and/or pattern of the rash.
  - Sequence (timeline) of events.
  - Associated hallmarks of infection.
  - Vaccine-preventable infection is most likely to develop in an unvaccinated child. (For example, in a new immigrant or in an adoptee.)
- **Remember: Any** rash may be itchy.

RUBEOLA (MEASLES)

A 6-year-old girl has a 1-day history of a rash that started on her face and spread to her trunk. Prior to developing the rash, she had a 4-day history of runny nose, pink eyes with crusting, barking cough, and high fever. She was never immunized because of her parents' beliefs. On exam, her temperature is 103°F (39.4°C), and there is a maculopapular rash most prominent on the trunk. Three tiny, whitish, round spots are present on her buccal mucosa. *Think: Measles.*

Measles is characterized by high fever, an enanthem (Koplik's spots), cough, coryza, conjunctivitis, and a maculopapular rash (exanthema). The rash usually begins on the face and appears several days after the initial symptoms. Koplik's spots precede the onset of rash.

TABLE 10-2. **1993 Centers for Disease Control and Prevention Clinical Classification of HIV Infection in Children < 13 years**

CLINICAL CATEGORY	DIAGNOSTIC CRITERIA
Not symptomatic	If two positive results on separate occasions
Mildly symptomatic	Two or more of following conditions: ■ Lymphadenopathy ■ Hepatomegaly ■ Splenomegaly ■ Dermatitis ■ Parotitis ■ Recurrent or persistent upper respiratory infections, sinusitis, or otitis media
Moderately symptomatic	■ Anemia, neutropenia, or thrombocytopenia persisting for 30 days ■ Bacterial meningitis, pneumonia, or sepsis ■ Candidiasis persisting > 2 months in child > 6 months ■ Cardiomyopathy ■ Cytomegalovirus infection ■ Hepatitis ■ Herpes zoster: two episodes in more than one dermatome ■ Disseminated varicella ■ Herpes simplex virus bronchitis, pneumonitis, or esophagitis ■ Nephropathy ■ Persistent fever (> 1 month) ■ Toxoplasmosis
Severely symptomatic	■ Serious bacterial infection (two in 2 years' time) ■ Disseminated coccidioidomycosis ■ Extrapulmonary cryptococcosis ■ Encephalopathy: more than one finding for > 2 months with no illness to explain ■ Disseminated histoplasmosis ■ Kaposi sarcoma ■ Primary lymphoma in brain ■ Tuberculosis ■ Other mycobacterium infection ■ *Pneumocystis jiroveci* pneumonia ■ Polymorphonuclear leukocytes ■ Wasting syndrome

ETIOLOGY

Paramyxovirus (RNA virus).

SIGNS AND SYMPTOMS

■ High fever and the "3Cs" (see Table 10-2) **precede** rash (3–5 days).
■ Conjunctivitis is exudative (yellow discharge).
■ Cough is croupy (barking, or "seal-like").

F I G U R E 1 0 - 2 . Koplik spots (rubeola). (Reproduced, with permission, from Knoop KJ, Stack LB, and Storrow AB. *Atlas of Emergency Medicine,* 1st ed. New York, NY: McGraw-Hill, 1997: 174.)

- Rash starts as faint macules on upper lateral neck, behind ears, along hairline, and on cheeks.
- Lesions become maculopapular and spread quickly downward ("shower distribution"), while the rash becomes confluent (erythrthroderma) starting from the top.
- Lymphadenopathy or splenomegaly may be present.
- **Koplik spots** (pathognomonic): Irregularly shaped spots with grayish, whitish, or bluish centers on buccal mucosa (see Figure 10-2).

DIAGNOSIS

- Clinical.
- Laboratory evaluation rarely necessary for diagnosis but important for confirmation and surveillance.

COMPLICATIONS

- Diarrhea (most common).
- Otitis media.
- Pneumonia (may be fatal in HIV patients).
- Encephalitis—most feared complication.

TREATMENT

- Supportive.
- The World Health Organization recommends vitamin A for all children with measles, regardless of their country of residence.

VACCINE

- Live attenuated vaccine included in measles-mumps-rubella (MMR) vaccine does NOT have any association with autism.
- Generally given at 12–15 months with a booster given at 4–6 years.

RUBELLA

> 👤 A 3-year-old girl develops a rash. She was recently adopted from Romania, and her immunization history is unknown. She is brought in because of a fever for 1 day. On physical examination, she is not ill-appearing, her temperature is 100.4°F (38.0°C), and there is a confluent maculopapular rash on her face and discrete rash on her trunk. Suboccipital and posterior cervical lymph nodes are palpable. WBC 7.2. *Think: Rubella.*
>
> Rubella has a prodrome of low-grade fever, sore throat, red eyes, headache, malaise, and anorexia. Suboccipital or postauricular lymphadenopathy is common. Rash is usually the first symptom, which appears on the face and spreads centrifugally to the extremities.

Rubella is contagious from 1 week before the rash appears to 1 week after it fades.

ETIOLOGY

Togavirus (RNA virus).

SIGNS AND SYMPTOMS

- Mild fever prodrome for 1–2 days.
- Rash begins on face and spreads quickly to trunk ("shower distribution"). As it spreads to trunk, it clears on face.
- Lymphadenopathy (retroauricular, posterior cervical, and suboccipital).
- Conjunctivitis may be present.
- Polyarthritis common in adolescent females.

COMPLICATIONS

- Progressive panencephalitis (very rare):
  - Insidious behavior change.
  - Deteriorating school performance.
  - Later, dementia and multifocal neurologic deficits.
- Thrombocytopenia (rare).

TREATMENT

Supportive; usually lasts about 3 days.

CONGENITAL RUBELLA SYNDROME

- The reason for rubella immunization is to prevent this syndrome. The earlier in gestation rubella occurs, the higher the risk of complications—more than 80% in the first trimester, and 25% at the end of the second trimester.
- Neonatal manifestations often severe:
  - Intrauterine growth retardation.
  - Pneumonitis.
  - Radiolucent bone lesions.
  - Hepatosplenomegaly.
  - Thrombocytopenia and **"Blueberry muffin"** rash (extramedullary erythropoiesis).
- Eye: Cataracts, glaucoma, pigmentary retinopathy, microphthalmos.
- Heart: Patent ductus arteriosus (PDA), peripheral pulmonary artery stenosis.
- Sensorineural hearing impairment.
- Neurologic: Meningoencephalitis, intellectual disability.

VACCINE

- Live attenuated vaccine included in MMR vaccine.
- Generally given at 12–15 months with a booster given at 4–6 years.

ROSEOLA

> An 11-month-old boy has had a fever 103–104°F (39.4–40ºC) for 4 days and was seen in ED because of febrile seizures. He had no vomiting, did not look sick, and his neurologic examination was normal. The only finding at the time was small suboccipital lymph nodes. No workup was done. One day later, the child's fever has resolved, but now he has a maculopapular rash. *Think: Roseola.*
>
> Roseola is associated with high fever for 3–5 days. There is a high association with febrile seizures. Rash appears when the fever disappears. Mild cervical or occipital lymphadenopathy may be present.

ETIOLOGY

- Human herpesvirus types 6 and 7.
- By the age of 4 years, almost all children are immune.

SIGNS AND SYMPTOMS

- High fever (may exceed 104°F).
- Mild upper respiratory symptoms or (commonly) no symptoms other than fever.
- Cervical and suboccipital lymphadenopathy.
- Maculopapular rash that spreads to the neck, face, and proximal extremities.

TREATMENT

Supportive (antipyretics, ↑ oral fluid intake, rest).

FIFTH DISEASE (ERYTHEMA INFECTIOSUM)

> An 8-year-old girl has a 4-day history of fever and bright red cheeks. Now she has rash everywhere and complains of knee pain. On examination, she is not sick-appearing, her temperature is 100.8°F (38.2°C), and she has "slapped"-looking cheeks and a discrete macular rash on the trunk and extremities that looks lacy. Her joints are intact with full range of motion. *Think: Erythema infectiosum, Parvovirus B19.*
>
> Erythema infectiosum is a self-limiting exanthematous illness in children. **Slapped-cheek** appearance is the classic presentation. In addition, a lacy, reticulated appearance on the extremities is often present.

ETIOLOGY

Parvovirus B19.

PATHOPHYSIOLOGY

- Attacks red blood cell precursors.
- Transmitted in respiratory secretions.

SIGNS AND SYMPTOMS

- Prodrome: 1 week of low-grade fever, headache, malaise, myalgia, and mild upper respiratory symptoms.
- **"Slapped cheeks,"** circumoral pallor.

- Rash spreads rapidly to trunk and extremities in ornamental **"lacelike"** pattern.
- Arthritis (knee), rare in children.

DIAGNOSIS

- Clinical (serum parvovirus B19 immunoglobulin M is available, e.g., for arthritis cases).
- Parvovirus B19 serology may be offered to women of childbearing age in frequent contact with children to determine their susceptibility to infection (e.g., teachers).

COMPLICATIONS

- Transient **aplastic crisis** in patients with chronic hemolysis including sickle cell disease (SCD), thalassemia, hereditary spherocytosis, and pyruvate kinase deficiency.
- Chronic anemia/pure red cell aplasia in immunocompromised hosts.
- Infection during pregnancy may lead to **hydrops fetalis:** Generalized edema due to fetal congestive heart failure (caused by fetal anemia).

TREATMENT

- Supportive (antipyretics, ↑ oral fluid intake, rest).
- Intravenous immune globulin (IVIG) should be considered for immunocompromised patients.

SCARLET FEVER

A 7-year-old boy has a sore throat, fever, and rash. His classmate had similar symptoms 1 week ago. On examination, his temperature is 102°F (38.9°C). He has red tonsils, swollen, tender bilateral anterior cervical lymphatic nodes (2.5 cm), and a confluent red rash that feels "sandpaper-like." He has circumoral pallor (nasolabial triangle and chin are spared). *Think: Scarlet fever.*

Scarlet fever has an abrupt onset of fever, chills, malaise, and sore throat with a distinctive rash that begins on the chest. Circumoral pallor is often present. The rash has a rough, sandpaper-like texture.

EXAM TIP

Scarlet fever common findings:
- Sandpaper rash
- Pastia lines
- Desquamation

ETIOLOGY

Erythrogenic exotoxins of group A β-hemolytic *Streptococcus* (GAS).

SIGNS AND SYMPTOMS

- Fever, often with sore throat.
- Confluent erythematous (erythroderma) **sandpaper-like rash.**
- Rash spares nasolabial triangle and chin **(circumoral pallor).**
- Accentuation of rash in a linear pattern in skin creases **(Pastia lines).**
- Desquamation **(peeling),** starting with fingers, in the second week.

DIAGNOSIS

- Clinical.
- Throat culture, anti-streptolysin O (ASO), and deoxyribonuclease B titers.

COMPLICATIONS

Rheumatic fever.

TREATMENT

Penicillin.

RHEUMATIC FEVER (SEE ALSO CARDIOVASCULAR DISEASE CHAPTER)

A 14-year-old girl presents after recently immigrating from Central America with fatigue, a swollen, painful knee, and a truncal rash. She has no known medical history but indicates that she had a sore throat for a few weeks prior to leaving her home country. *Think: Rheumatic fever.*

Rheumatic fever is a diagnosis based on Jones criteria.

ETIOLOGY

Sequelae of untreated rheumatogenic group A β-hemolytic *Streptococcus* (GAS).

SIGNS AND SYMPTOMS

Nonspecific and due to the individual, particular manifestations of disease.

DIAGNOSIS

- Jones criteria: Based on evidence of recent Group A *Streptococcus* infection plus two major or one major and two minor criteria.
- Major criteria:
  - Arthritis.
  - Carditis—most commonly affecting the mitral valve followed by the aortic valve.
  - Subcutaneous nodules.
  - Erythema marginatum.
  - Syndenham's chorea.
- Minor criteria: Arthralgia, fever, elevated ESR or CRP, prolonged PR interval.

TREATMENT

Long-acting PCN (Bi-Cillin) every 4 weeks.

VARICELLA (CHICKENPOX)

A 5-year-old boy has had a fever for 3 days and an itchy rash that started yesterday. He is a recent immigrant from overseas. On examination, his temperature is 101.8°F (38.8°C) and he does not look sick. There are crops of papules, vesicles, pustules, and crusts on his face, trunk, and extremities. *Think: Varicella.*

Varicella is a highly contagious disease characterized classically by a prodrome of URI symptoms followed by a generalized, vesicular, pruritic rash with a centripetal distribution. In a patient with chickenpox, erythematous macules, papules, vesicles, and scabbed lesions are present in various stages simultaneously.

DEFINITION

Highly contagious, self-limited viral infection characterized by multiple pruritic vesicles (Figure 10-3).

ETIOLOGY

Varicella-zoster virus (VZV), group of herpesviruses.
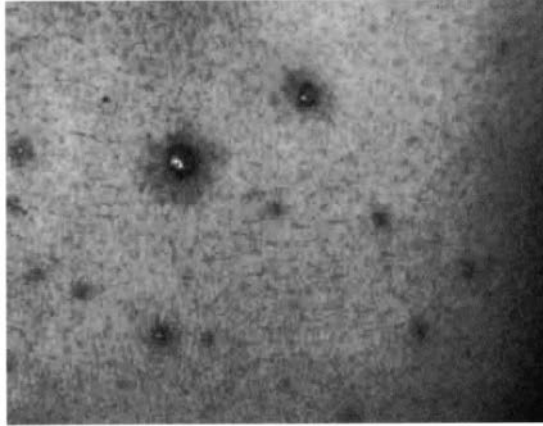
F I G U R E 1 0 - 3 . **Varicella (chickenpox).** Note dewdrop appearance of lesion and that there are lesions in multiple stages of eruption.

EPIDEMIOLOGY

- Ninety percent of patients are <10 years old.
- There is often a history of exposure to an infected individual.
- Incidence is ↓ since introduction of varicella vaccine.

PATHOPHYSIOLOGY

- Transmitted by respiratory secretions and fluid from the skin lesions.
- Replicates in the respiratory tract.
- Establishes lifelong infection in sensory ganglia cells.

SIGNS AND SYMPTOMS

- May have a prodrome of fever, with URI symptoms or with malaise, anorexia, headache, and abdominal pain 24–48 hours before the onset of the rash.
- **"Dew drops on a rose petal"** (vesicles with an erythematous base) initially appear on face and spread to trunk and extremities, **sparing palms and soles.**
- Within days, vesicles become turbid and then crusted (see Figure 10-3).

DIAGNOSIS

- Clinical; Tzanck preparation is **not** used anymore.
- PCR test of swab from the vesicle.

COMPLICATIONS

- Skin lesions may be superinfected by bacteria (*Streptococcus pyogenes* or *Staphylococcus aureus*). For unknown reasons, these skin superinfections may lead to severe complications like necrotizing fasciitis.
- Pneumonia in immunocompromised or pregnant patients.
- Encephalitis.
- **Reye syndrome** (associated with aspirin use).

TREATMENT

- For most immunocompetent children: Symptomatic for fever and pruritus.
- For VZV pneumonia and for immunocompromised individuals: Acyclovir.

CONGENITAL VARICELLA SYNDROME

Caused by maternal varicella infection in **first 20 weeks** of pregnancy.

WARD TIP

Herpes zoster (shingles) is the reactivation of VZV from nerve ganglia and occurs in dermatomal distributions.

WARD TIP

Smallpox generally presents with all lesions in the same stage (compared with chickenpox with lesions at various stages).

WARD TIP

Varicella-zoster immune globulin (VZIG) is used for post-exposure prophylaxis in immunocompromised or newborns exposed to maternal varicella.

SYMPTOMS

- **Cicatricial** skin lesions (cutaneous scarring).
- **Limb hypoplasia.**
- Neurologic deficits.
- Eye abnormalities.

VACCINE

Live attenuated vaccine, first dose given between 12 and 18 months of age, second dose age >4 years.

HAND-FOOT-MOUTH DISEASE

ETIOLOGY

Enteroviruses—specifically coxsackie virus.

EPIDEMIOLOGY

- Fecal-oral and respiratory routes of infection.
- Summer and fall seasonal pattern exist against a background of year-round disease.

SIGNS AND SYMPTOMS

- GI discomfort.
- Ulcerative mouth lesions (small, superficial, round erosions).
- Hand and foot lesions are tender and vesicular.
- Hands more commonly involved than feet. May be ONLY oral.
- May occur on **palms and soles.**

COMPLICATIONS

- Aseptic meningitis.
- Encephalitis.

MUMPS

An unvaccinated 14-year-old boy presented with fever of 100.9°F (38.3°C), bilateral facial swelling, and inability to eat normally because of pain when he tried to chew. On examination, he was active and had trismus (inability to open wide the mouth) and swelling in front of the earlobes. There was no redness or purulent discharge at Stenson duct openings. At a follow-up visit 8 days later, his parotid swelling has resolved, but now he has a swollen, tender left testis. *Think: Mumps orchitis.*

Parotid swelling is the classic feature of mumps. Parotitis is often accompanied by a prodrome of low-grade fever, myalgias, and anorexia. Epididymo-orchitis is a common extra–salivary gland complication of mumps in postpubertal males. It is characterized by marked testicular swelling and severe pain and may be associated with fever, nausea, and headache. Testicular atrophy may follow, although sterility is not common.

ETIOLOGY

Paramyxovirus (RNA virus).

PATHOPHYSIOLOGY

- Spread via respiratory secretions.
- Incubation period of 14–24 days.

SIGNS AND SYMPTOMS

- Rare viral prodrome.
- Swelling and tenderness in one or both parotid glands.
- Difficulty opening the mouth (trismus).

COMPLICATIONS

- Meningoencephalomyelitis (rare).
- Orchitis/oophoritis common after puberty.
- Pancreatitis.
- Arthritis.
- Thyroiditis.
- Deafness.

VACCINE

- Live attenuated vaccine included in MMR vaccine.
- Generally given at 12–15 months with a booster given at 4–6 years.

Bacterial Infections

TYPHOID (ENTERIC) FEVER

An 8-year-old boy develops a fever 5 days after returning from Africa. The fever escalates in the next 7 days. He develops abdominal pain and refuses to eat. His last bowel movement occurred prior to the onset of fever and was normal. On examination, his temperature is 103°F (39.4°C), HR 68 beats/min. There are fine pink spots on the abdomen and a palpable spleen (2.5 cm). Abdomen is soft, with mild, inconsistent tenderness and no guarding or rebound. WBC is 2.9 and blood smear shows no parasites. *Think: Typhoid fever.*

Typhoid fever is characterized by a prolonged fever, relative bradycardia, splenomegaly, rose spots, and leukopenia. It is caused by infection with *Salmonella typhi*.

> **EXAM TIP**
>
> Typhoid fever:
> - Relative bradycardia
> - Rose spots
> - Hepatosplenomegaly

ETIOLOGY

Salmonella typhi.

PATHOPHYSIOLOGY

- Fecal-oral transmission.
- Incubation period of 7–14 days.
- Time of incubation is dependent on inoculum size.

SIGNS AND SYMPTOMS

- **Fever:** Gradual rise in the first week, gradual decrease in the third week.
- Malaise.
- Anorexia.
- Myalgia.
- Headache.
- Abdominal pain.
- Diarrhea is a late sign.
- **Transient rose-colored spots on trunk.**
- Hepatosplenomegaly.

COMPLICATIONS

- Intestinal hemorrhage.
- Intestinal perforation.
- Sepsis.

DIAGNOSIS

- Blood, urine, and stool cultures.
- Blood culture sensitivity is ~60%.

TREATMENT

- Ceftriaxone.
- Consider dexamethasone for severe cases with altered mental status.

VACCINE

Available for travelers to endemic areas (not routinely recommended).

TICK-BORNE INFECTIONS

Lyme Disease

A 6-year-old boy develops limping, swelling, and pain in his right knee; there is no fever. Physical examination shows temperature of 98.6°F and no distress. There is no rash, murmur, or organomegaly. The right knee is swollen and warm, but not red, with ↓ range of motion due to pain on passive movement. *Think: Lyme disease vs. reactive or post-viral arthritis.*

An 11-year-old girl presents with an enlarging erythematous, non-itchy spot on her left shoulder. She was camping in upstate New York 2 weeks ago. On examination, her temperature is 100.3°F (37.9°C), she is not sick-appearing, and she has a flat annular lesion 7 cm in diameter on the left shoulder. No regional lymphadenopathy is noted. *Think: Lyme disease.*

Lyme disease is a tick-borne, inflammatory disorder due to the spirochete *Borrelia burgdorferi*. The most common manifestation of Lyme disease in children is erythema migrans rash and arthritis. Most cases of Lyme disease are from the Mid-Atlantic states and upper Midwest.

DEFINITION

A multisystem disease transmitted by the bite of an *Ixodes* tick infected with spirochetes.

ETIOLOGY

Borrelia burgdorferi.

EPIDEMIOLOGY

- Patients are often unaware of the tick bite.
- Incubation period: 2–31 days (see Table 10-3).
- Keep in mind geography (presence of a vector) and season (see Table 10-4).

PATHOPHYSIOLOGY

Disseminated Lyme is due to spirochetemia.

TABLE 10-3. **Fever and Rash**

INFECTION	SEQUENCE OF EVENTS	PRIMARY ELEMENT(S) OF RASH	DISTRIBUTION, PATTERN	HALLMARKS
Measles (rubeola)	Fever and **"3Cs"** × 3–4 days **precede rash: C**oryza, **C**onjunctivitis, **C**ough (barking)	Maculopapular	**"Shower"** from the top down Becomes confluent, also from the top	**Koplik's spots** on buccal mucosa
Rubella	Low-grade fever may start 1–2 days prior to rash	Maculopapular	**"Shower"** from the top down	Suboccipital lymphatic nodes
Roseola (HHV 6,7) (exanthem subitum)	**High** fever 4–5 days; rash appears **after** fever has resolved	Maculopapular	Discrete, may last just for a few hours	Febrile seizures, suboccipital lymphatic nodes, red eardrums
Erythema infectiosum (Parvovirus B19) (fifth disease)	Fever and malaise prodrome, then red **("slapped")** cheeks	Maculopapular	**Lacelike, fluctuates** over time with room temperature changes	Rare arthritis, knee; aplastic crisis in sickle cell disease; hydrops fetalis in pregnancy
Scarlet fever (erythrotoxin of group A *Streptococcus*)	Exactly "red fever," often with sore throat, × 7 days; desquamation **(peeling)** in week 2	**Sandpaper**-feeling confluent redness of the skin (erythroderma)	Accentuated in **folds,** where darker **Pastia's lines** are seen	Nasolabial triangle and chin are spared **("circumoral pallor");** high anti-streptolysin O, positive throat culture
Varicella	**Crops** of **"dew drops on a rose petal"** appear over 3–7 days, with fever	Evolution from papule to vesicle to pustule to excoriation	**Rash in the different stages of evolution;** palms and soles spared	May be associated with meningitis or encephalitis
Hand-foot-mouth disease (coxsackievirus A16)	Fever, rash, with or without sore throat, upper respiratory/gastrointestinal infection symptoms	Macules, papules, **vesicles**	**Palms and soles** involved	Enanthema: Erosions on the pharynx, palate, tongue

SIGNS AND SYMPTOMS

- See Table 10-4.
- **Erythema chronicum migrans (ECM):**
    - Begins as a red macule or papule that gradually (over days to weeks) turns into an annular, erythematous lesion of 5–15 cm in diameter (Figure 10-4).
    - Sometimes there is partial central clearing ("bull's eye" appearance).
    - May have vesicular or necrotic areas in its center and can be confused with cellulitis.
    - Usually is painless and not pruritic.
    - May be located at the axilla or in the groin. Not necessarily found at the site of the bite.
    - May be associated with acute onset of fever, chills, myalgia, weakness, headache, and photophobia.

TABLE 10-4. Stages of Lyme Disease

| STAGE | EARLY LOCALIZED | EARLY DISSEMINATED | | | LATE | |
		MULTIPLE EM	CARDITIS	MENINGITIS	ARTHRITIS	POLYRADICULONEUROPATHY
Time after tick bite	2–31 days	3–5 weeks			> 6 weeks	
Clinical features	**EM,** headache, fever, myalgia	Most common	Rare Heart block	Benign CSF: Lymphocytic	Knee, may be relapsing course	Rare Gloves-and-socks: Pain, paresthesias
Diagnosis	Clinical	Serology		Serology, CSF: IgM, PCR	Serology, synovial PCR	Serology
Treatment	Amoxicillin or cefuroxime **Doxycycline: After 8 years of age**	Ceftriaxone or penicillin **IV**			**Acute:** Amoxicillin, doxycycline **Persistent:** Ceftriaxone or penicillin **IV**	Ceftriaxone or penicillin **IV**

CSF, cerebrospinal fluid; EM, erythema migrans; IgM, immunoglobulin M; PCR, polymerase chain reaction.

FIGURE 10-4. Erythema chronicum migrans rash characteristic of Lyme disease.

- **Isolated facial palsy** (CN VII, Bell's palsy): Develops 3–5 weeks after exposure.
    - Treatment of Lyme does not affect resolution of facial palsy, but prevents late events (arthritis).
    - Self-limited and may be bilateral.

DIAGNOSIS

- Confirmed by serology.
- During the first 4 weeks of infection, serologic tests are negative and therefore not recommended.

- Immunoglobulins M and G (IgM and IgG) peak 4–6 weeks after exposure and are detected by **ELISA** (**screening**, may be **false positive**) and **Western immunoblot (confirmation).**
- False-positive results with other spirochetal infections (syphilis, leptospirosis) and in patients with some autoimmune disorders (lupus, rheumatoid arthritis).
- An elevated IgG titer in the absence of an elevated IgM indicates prior exposure as opposed to recent infection.
- PCR can detect spirochete DNA in CSF and synovial fluid.

COMPLICATIONS

- Arthritis—will develop in 60% of patients if left untreated.
- Carditis—can be evidenced by heart block (most common).
- Meningitis—requires prolonged period of parenteral treatment.

TREATMENT

- **Amoxicillin, cefuroxime, or doxycycline:**
    - EM: 14–21 days.
    - Multiple EM: 21 days.
    - Isolated facial palsy: 21–28 days.
    - Arthritis: 28 days.
- **Ceftriaxone or penicillin IV:** Carditis, meningitis, persistent/recurrent arthritis: 14–28 days.

Rocky Mountain Spotted Fever (RMSF)

> An 8-year-old girl from North Carolina presents with fever, severe headache, and myalgia over 3 days in July. She attended a family picnic 1 week ago. On examination, she has a temperature of 102.9°F (39.4°C), HR 134 beats/min. She is complaining of headache and has a macular rash on her wrists, palms, ankles, and soles. There are no other significant findings. Her platelets are 68 and serum sodium is 129. *Think: Rocky Mountain spotted fever.*
>
> RMSF is a systemic tick-borne illness caused by *Rickettsia rickettsii.* Rash is considered the hallmark of this disease, which characteristically involves the palms and soles. Severe frontal headache is common. Abdominal pain, splenomegaly, and conjunctivitis may also be present. Highest incidence rates for RMSF are in North Carolina, Oklahoma, Arkansas, Tennessee, and Missouri. Classic laboratory abnormalities include thrombocytopenia, hyponatremia, and elevated liver enzymes.

DEFINITION

A potentially life-threatening disease transmitted by the bite of a *Dermacentor* tick infected with bacteria.

ETIOLOGY

Rickettsia rickettsii.

EPIDEMIOLOGY

Keep in mind geography (presence of a vector) and season (see Table 10-4).

PATHOPHYSIOLOGY

- An **intracellular infection of the endothelial cells** lining the small blood vessels, resulting in vascular necrosis and extravasation of blood.
- Only 60% of patients report a history of a tick bite.
- The **incubation period** is 2–14 days.

WARD TIP

If untreated, lesions fade within 28 days. If delayed diagnosis, may have permanent neurologic or joint disabilities.

WARD TIP

If treated adequately, lesions fade within days and the late manifestations are prevented.

- **Rarely** occurs in the Rocky Mountains.
- **Highest incidence in children 5–10 years old.**

SIGNS AND SYMPTOMS

- Sudden onset of high fever, myalgia, severe headache, rigors, nausea, and photophobia.
- Fifty percent develop rash within 3 days. Another 30% develop the rash within 6 days.
- Rash consists of 2- to 6-mm pink initially **blanchable macules** that first appear peripherally on wrists, forearms, ankles, **palms,** and **soles.**
- Within 6–18 hours the exanthem spreads centrally to the trunk, proximal extremities, and face (centrifugal).
- Within 1–3 days the macules evolve to deep-red papules, and within 2–4 days the exanthem is hemorrhagic, petechial, and no longer blanchable.
- **Up to 15% have no rash** ("spotless").
- Many patients have exquisite tenderness of the gastrocnemius muscle.
- Meningitis is common.
- If untreated, myocarditis, disseminated intravascular coagulation (DIC), and shock can result, with fatality rate up to 25%.

DIAGNOSIS

- Clinical.
- Rash biopsy would demonstrate necrotizing vasculitis.
- Indirect fluorescent antibody (IFA) assay: Titer >1:64 is diagnostic.

TREATMENT

Doxycycline, regardless of patient's age.

COMPLICATIONS

- Noncardiogenic pulmonary edema.
- Meningoencephalitis.
- Multiorgan damage due to vasculitis.

TOXIC SHOCK SYNDROME

DEFINITION

An acute, febrile, exanthematous illness that involves multiple systems with potential complications that include shock, renal failure, myocardial failure, and acute respiratory distress syndrome (ARDS).

PATHOPHYSIOLOGY

- Hematogenous dissemination of an endotoxin.
- Toxins from *Staphylococcus* or *Streptococcus* (Table 10-5) act as superantigens activating T cells nonspecifically, resulting in massive release of cytokines with profound physiologic consequences (i.e., fever, vasodilation, hypotension, and multisystem organ involvement).

SIGNS AND SYMPTOMS

- Ill-appearing patient.
- Diffuse erythroderm is classic.
- Staphylococcal TSS (*S. aureus*): **Less than half is associated with menstrual tampons.** Source also may be nasal or wound packing, or an abscess.
- Streptococcal TSS (group A *Streptococcus*): Usually there is evidence of soft tissue infection (see Table 10-6), classically **necrotizing fasciitis in a patient with varicella.**

TABLE 10-5. Epidemiology of Tick-Borne Infections

INFECTION	GEOGRAPHY (UNITED STATES)	TICK (VECTOR)	SEASON
Lyme borreliosis	Upper East Coast: New Hampshire to Virginia	*Ixodus scapularis*	April–October
	Upper Midwest: Wisconsin, Minnesota West Coast: California	*Ixodus pacificus*	
Rocky Mountain spotted fever	Western states	*Dermacentor andersoni* (wood tick)	May–September
	Southeast: North Carolina, South Carolina	*Dermacentor variabilis* (American dog tick)	
	South central: Tennessee, Oklahoma Arizona	*Rhipicephalus sanguineus* (brown dog tick)	

TABLE 10-6. Diagnostic Criteria of Toxic Shock Syndrome (TSS)

STREPTOCOCCAL **TSS**	STAPHYLOCOCCAL **TSS**
Isolation of GAS (throat, wound, blood) and hypotension	1. T > 102°F
And > 2 signs:	2. Diffuse erythroderma
▪ **Soft tissue necrosis** (fasciitis, gangrene)	3. Desquamation in **week 2 (hands)**
▪ ARDS	4. Hypotension
▪ Erythroderma, desquamation	**And > 3 signs:**
▪ Renal (creatinine)	▪ **Vomiting/diarrhea at onset**
▪ Liver (transaminases)	▪ Myalgia or elevated CPK
▪ Coagulopathy (thrombocytopenia, DIC)	▪ **Red mucosae** (oropharyngeal, vaginal, conjunctival)
	▪ CNS: altered mental status
	▪ Renal (creatinine)
	▪ Liver (transaminases)
	▪ Thrombocytopenia

ARDS, adult respiratory distress syndrome; CPK, creatine phosphokinase; DIC, disseminated intravascular coagulation; GAS, group A *Streptococcus.*

▪ Nikolski sign (see Dermatologic Disease chapter) is present in staphylococcal scalded skin syndrome and is characterized by sloughing of intact skin with minor shearing force.

TREATMENT

▪ Aggressive fluid replacement.
▪ Eradication of infectious source.
▪ Parenteral β-lactamase-resistant antibiotic plus **clindamycin** (reduces toxin synthesis).
▪ Recovery in 7–10 days with appropriate treatment.

Fungal Infections

See Table 10-7 for a summary of endemic fungal infections.

TABLE 10-7. **Streptococcal versus Staphylococcal**

	GROUP A *STREPTOCOCCUS*	*STAPHYLOCOCCUS AUREUS*
Prodrome	Flulike	*Vomiting, diarrhea*
Focal infection	Soft tissue	Sometimes—wound
Erythroderma	Rare	Yes
Positive blood culture	60%	Rare

COCCIDIOIDOMYCOSIS

A 13-year-old girl develops fever, cough, and chest pain. On examination, her temperature is 102.5°F (39.2°C), RR 44 breaths/min, no hypoxemia, and rales are heard over her left lower lobe. There are symmetrical tender, red, shiny indurations on both shins. WBC: 16.8. Chest radiograph shows left lower lobe consolidation. Further history-taking reveals recent trip to Arizona. *Think: Coccidioidomycosis.*

Coccidioidomycosis is an infectious disease caused by the fungus *Coccidioides immitis.* Also known as San Joaquin Valley fever, coccidioidomycosis should be considered in southwestern U.S. states (Arizona, California, Nevada, New Mexico, Utah, and Texas). Symptoms usually develop 1–3 weeks after exposure. Clinical features include dry cough, chest pain, myalgia, arthralgia, fever, anorexia, and weakness. Infection is often subclinical.

ETIOLOGY

Coccidioides immitis.

EPIDEMIOLOGY

- Southwestern United States.
- Black and Filipino, pregnant women, neonates, and immunocompromised people have higher risk of disseminated disease.
- Incubation period: 1–3 weeks.
- Transmission: Inhalation of airborne spores.
- Person-to-person transmission **does not occur.**
- Infection produces **lifelong immunity.**

SIGNS AND SYMPTOMS

- Usually asymptomatic or self-limited: Influenza-like or pneumonia, with fever, cough, headache, malaise, myalgia, and chest pain. May also have night sweats and anorexia.
- Maculopapular rash, erythema multiforme, or erythema nodosum may be the only manifestations.
- Dissemination is rare, mostly in infants or immunocompromised patients: Skin, bones and joints, central nervous system (CNS), and lungs.
- Meningitis almost invariably is fatal if untreated.

DIAGNOSIS

- Coin-like pulmonary lesions may be present on chest x-ray.
- **Spherules with endospores** in tissue or body fluid is pathognomonic.

- Laboratory diagnosis with serology (IgG and IgM) or cultures (may be infectious).
- Elevated erythrocyte sedimentation rate (ESR) and alkaline phosphatase.
- Marked eosinophilia.

TREATMENT

- Fluconazole or itraconazole.
- Surgical resection for chronic pulmonary coccidioidal disease that is unresponsive to IV azole or amphotericin B therapy.

HISTOPLASMOSIS

A 6-year-old boy from Indiana develops fever, chest pain, and cough. He was playing in a cave 10 days ago and got scared by bats. Physical exam shows no distress, temperature of 100.7°F (38.2°C), RR 28 breaths/min, oxygen saturation 95%. Rhonchi are heard over the lung fields bilaterally. WBC: 14.9. Chest x-ray shows bilateral diffuse reticulonodular infiltrates and hilar lymphadenopathy. *Think: Histoplasmosis.*

Histoplasmosis is the most common endemic mycosis causing human infection. Pneumonia is the most common presentation, and atypical pneumonia is usually the initial diagnosis. Initial chest x-ray may show patchy infiltrates, while diffuse reticulonodular infiltrates are present in progressive disease. The presence of hilar or mediastinal lymphadenopathy increases the suspicion for fungal pneumonia.

ETIOLOGY

Histoplasma capsulatum.

EPIDEMIOLOGY

- **Endemic** infection: Ohio and Mississippi River valleys.
- History of exposure to **bird or bat droppings.**
- Incubation period: 1–3 weeks.
- Transmission: Inhalation of airborne spores.
- Reinfection may happen with large inoculum.

SIGNS AND SYMPTOMS

- Generally asymptomatic.
- Flulike prodrome.
- The more spores inhaled, the more symptoms.
- Severe acute pulmonary infection: diffuse nodular infiltrates, prolonged fever, fatigue, and weight loss.
- **Progressive disseminated histoplasmosis:** In infants <2 years of age and in immunosuppressed, often starts as prolonged "fever of unknown origin."

DIAGNOSIS

- Mediastinal adenitis or granuloma may be seen on chest x-ray.
- *Histoplasma* antigen assay: Urine or serum; cross-reaction with other endemic fungi.
- Cultures: Sputum, blood, bone marrow; may be negative.

TREATMENT

- Uncomplicated infection in an immunocompetent child is self-limited and does not require treatment.
- Oral itraconazole for serious focal (pulmonary) infection.
- IV amphotericin B for progressive disseminated disease.

In order to recognize endemic fungal infection, keep in mind:

Geography	Setting
Timing	Hallmarks
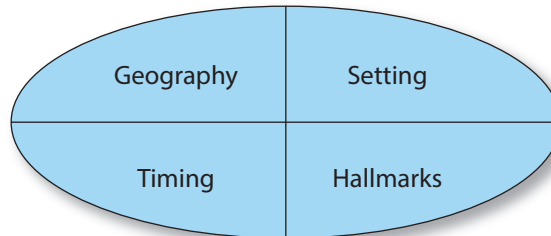
Protozoal Infections

SCHISTOSOMIASIS (SEE TABLE 10-8)

A 16-year-old male presents with fever, arthralgia, cough, abdominal pain, and rash for 5 days. He went to Puerto Rico for a river rafting trip 3 weeks ago. On examination, his temperature is 102°F (38.9°C), there are scattered urticaria on his trunk and extremities that wax and wane, and his spleen is palpable 3 cm below the costal margin. WBC count is 6.1, with 23% eosinophils. *Think: Schistosomiasis.*

Schistosomiasis is transmitted in tropical and subtropical areas. Clinical presentation includes fever, chills, cough, abdominal pain, diarrhea, nausea, vomiting, headache, rash, and lymphadenopathy. Physical examination may show an enlarged, nontender liver and an enlarged spleen. Eosinophilia is often prominent.

ETIOLOGY

Caused by trematodes (flukes).

EPIDEMIOLOGY

- Ova from urine or feces hatch to release miracidia, which penetrate snail tissue and grow into larvae (cercaria).
- Larvae leave the snail into the fresh water and penetrate the skin.
- After skin penetration, larvae travel to particular organs and tissues, and there develop into mature forms.

SIGNS AND SYMPTOMS

- "**Swimmer's itch**" transient, a few hours after water exposure, followed in 1–2 weeks by an intermittent pruritic, papular rash.
- Invasive stage: Within weeks to months of exposure—fever, malaise, cough, abdominal pain, and nonspecific rash.
- Ulceration of intestine and colon, abdominal pain, and bloody diarrhea (*Schistosoma interclatum* and *Schistosoma mekongi*; less common).

WARD TIP

Pay attention to travel history and timing from return (incubation period from weeks to months).

WARD TIP

Risk is exposure to fresh water (lake, river) in an endemic area: Swimming, fishing, playing.

T A B L E   1 0 - 8 .   **Summary of Endemic Fungal Infections**

	HISTOPLASMOSIS	**COCCIDIOIDOMYCOSIS**
Geography	Mississippi, Ohio, and Missouri River valleys	Utah, Arizona, New Mexico, Texas, California
Setting	Gardening, demolition, visiting **caves (bat droppings);** playing in barns, hollow trees with **bird roosts**	Dust storms, earthquakes, **archeologic digging,** picnic in a desert
Focal infection	Pulmonary infiltrates, hilar adenopathy In adolescents: **Erythema nodosum**[a]	Influenza-like or pneumonia: Fever, cough, headache, malaise, myalgia, and chest pain **Erythema multiforme** **Erythema nodosum**[a]
Disseminated infection	**Prolonged fever,** pneumonitis, lymphadenopathy, hepatosplenomegaly, failure to thrive or weight loss, meningitis, **pancytopenia**	**Rare** Skin: Papules, nodules **Osteomyelitis,** arthritis Meningitis, pneumonitis
Diagnosis	**Culture** of sputum, blood, bone marrow Histology: **Intracellular yeast** with silver stain	**Serology:** IgM and IgG Histology: **Spherules** in pleural fluid bronchoalveolar lavage, and skin biopsy specimens
Treatment Focal infection Disseminated infection	 Itraconazole Amphotericin B	 Fluconazole or itraconazole Amphotericin B

[a]Erythema nodosum is an inflammatory exanthem, an area of tender, red and shiny induration, usually on the shins.

DIAGNOSIS

- **Eggs** in stool or urine.
- Peripheral **eosinophilia.**

TREATMENT

Praziquantel.

TOXOCARIASIS

ETIOLOGY

Toxocara canis and *Toxocara cati* (roundworms of puppies or kittens).

EPIDEMIOLOGY

- Fecal-oral transmission: Eggs in soil make their way into the mouth by getting onto hands or toys.
- Role of **pica** (eating soil): Ingested eggs hatch and penetrate the GI tract, migrating to the liver, lung, eye, central nervous system, and heart, where they die and calcify.

SIGNS AND SYMPTOMS

- Most individuals are asymptomatic.
- Symptomatic in young children (under 4 years of age).

WARD TIP

Differentiate eye lesions of visceral larva migrans from retinoblastoma.

- The more larvae, the more symptoms.
- **Visceral:** Fever, cough, wheezing (pneumonitis), **hepatomegaly.**
- Rare: Myocarditis, encephalitis (seizures).
- **Ocular:** Endophthalmitis or retinal granulomas, **usually in older children** or adolescents.

Diagnosis

- **Leukocytosis** and **hypereosinophilia.**
- ELISA for *Toxocara* antibodies. ELISA is more sensitive in visceral than in ocular form of infection.

Treatment

Albendazole.

Traumatic Infections

ANIMAL BITES/SCRATCHES

- **Cleaning, debridement, and irrigation are the most important treatment.**
- Antibiotic prophylaxis for all human bites ("fight bites" on hands are particularly susceptible to infection and may require surgical debridement for tenosynovitis).
- Cat bites more likely to get infected than dog bites (puncture wounds of cat teeth deposit bacteria deeply). Prophylaxis for wounds on the hands, feet, or face. For other wounds base prophylaxis on degree of tissue damage.
- X-ray to check for bone involvement or foreign body if deep wound.
- Most wounds on extremities should **not** be sutured; if deep wounds, surgical consult should be considered.
- Assess risk for rabies using local epidemiological information.
- Antibiotic of choice is typically amoxicillin/clavulanic acid based on microbiology.
- Ensure **tetanus immunization** is up to date.

ABRASIONS AND LACERATIONS

A 10-year-old boy steps on a dirty nail that punctures his foot through his sneaker. Two days later he presents with pain, swelling, and redness of the heel, with purulent drainage from a central pinpoint opening. He has no fever. WBC is 14.6. X-ray shows no foreign body, no fracture, and no gas in the soft tissue. *Think: Wound likely to become infected with* Pseudomonas. The association of *Pseudomonas* infection with puncture wounds to the foot is well recognized.

- **Cleaning, debridement, and irrigation are most important initial treatment**. Suturing to be considered, but increases risk of infection so must weigh against cosmetic outcome.
- If secondarily infected, debride and drain.
- Antibiotic prophylaxis generally not indicated unless wound is heavily soiled or large amount of tissue damage; gram stain and culture to determine best antibiotic in chronic or complex wounds.

- *Staphylococcus* and *Streptococcus* are the most common pathogens, so a first-generation cephalosporin such as cephalexin or clindamycin is commonly given as empiric treatment.
- *Pseudomonal* coverage must be added if puncture wound through shoe, and ensure tetanus immunization is up to date.

Human Immunodeficiency Virus (HIV) in the Child

ETIOLOGY

- Infants: Vertical transmission from mothers either perinatally or through breast milk (preventable with antiretroviral prophylaxis).
- Adolescents: Sexual transmission or IV drug use.

CLINICAL PRESENTATION

- Suspect HIV infection in a child with failure to thrive, oral thrush after 3 months of age, generalized nontender lymphadenopathy, hepatosplenomegaly, and thrombocytopenia.
- Consider acute HIV syndrome in a sexually active adolescent with mononucleosis-like illness with fever, lymphadenopathy, and hepato-splenomegaly.
- See Table 10-9 for clinical classifications.

DIAGNOSIS

- HIV screening is part of prenatal care.
- In non-breast-feeding infants <18 months of age and born to HIV-infected mothers, *definitive* exclusion of HIV-1 is based on:
  - At least two negative **HIV-1 DNA or RNA virologic tests** obtained at ≥1 month of age and ≥4 months of age **OR**
  - Two negative HIV-1 **antibody test** results from separate specimens obtained at ≥6 months of age **AND**
  - No other laboratory or clinical evidence of HIV-1 infection, including no AIDS-defining illness for which there is no other underlying immunosuppression.
- In adolescents >13 years of age, rapid oral swab enzyme immunoassay (EIA) is an alternative diagnostic method. If it is positive, confirmatory enzyme-linked immunosorbent assay (ELISA) and Western blot are required.

EXAM TIP

Perinatal HIV
- Lymphadenopathy
- Hepatosplenomegaly
- Oral thrush
- Failure to thrive

EXAM TIP

Common presentation of HIV:
  Infants: PCP
  Children: ITP

TABLE 10-9. Schistosomiasis

	SCHISTOSOMA MANSONI	*SCHISTOSOMA JAPONICUM*	*SCHISTOSOMA HAEMATOBIUM*
Geography	Africa, Arabian Peninsula, Caribbean, Latin America	China, Indonesia, Philippines	Africa, eastern Mediterranean
Target	Mesenteric vessels	Liver	Urinary bladder
Presentation	**Hepatosplenomegaly, portal hypertension,** hematemesis, ascites		**Dysuria, hematuria,** bladder fibrosis, or cancer
Egg emboli	Lungs, spinal cord		Lungs, brain

TREATMENT

- Three classes:
    - Nucleoside reverse transcriptase inhibitors (NRTIs).
    - Non-nucleoside reverse transcriptase inhibitors (NNRTIs).
    - Protease inhibitors.
- HIV rapidly becomes resistant; therefore, multidrug therapy is necessary.

Common Opportunistic Infections in HIV

TOXOPLASMOSIS

ETIOLOGY

- *Toxoplasma gondii* (intracellular protozoan).
- Toxoplasma oocysts are classically present in cat feces.

SIGNS AND SYMPTOMS

- Mononucleosis-like syndrome including fever, lymphadenopathy, and hepatosplenomegaly.
- Disseminated infection with T-cell deficiency.

DIAGNOSIS

Serologic antibody tests, biopsy, visualization of parasites in CSF.

TREATMENT

Pyrimethamine and sulfadiazine used concurrently (both inhibit folic acid synthesis, so replace folic acid).

CRYPTOCOCCOSIS

DEFINITION

- Fungal infection.
- Primary infection in lungs.
- The fungus disseminates to brain, meninges, skin, eyes, and skeletal system in immune compromised individuals.

SIGNS AND SYMPTOMS

- Subacute or chronic meningitis is the most common presentation in AIDS.
- Typically presents with fever, headache, and malaise.
- Postinfectious sequelae common, including:
    - Hydrocephalus.
    - Change in visual acuity.
    - Deafness.
    - Cranial nerve palsies.
    - Seizures.
    - Ataxia.

DIAGNOSIS

- Definitive diagnosis requires isolation of the organism from body fluid or tissue specimens: Sputum, bronchopulmonary lavage (BAL), or CSF.
- **Niger seed (birdseed)** can ↑ detection in sputum and urine.
- The latex agglutination test and EIA for detection of **cryptococcal capsular polysaccharide antigen in serum or CSF** specimens are excellent rapid diagnostic tests.

- Microscopy: Encapsulated yeast seen as white halos when CSF is mixed with India ink.
- Can be grown in culture (takes up to 3 weeks).
- May also see cryptococcomas on head CT.

TREATMENT

- Treat with combination therapy using amphotericin B and flucytosine.
- Relapse rate is very high. This is a reason for subsequent maintenance therapy with oral fluconazole.

PNEUMOCYSTIS JIROVECII PNEUMONIA

Formerly *P. carinii*, now classified as a fungus.

EPIDEMIOLOGY

- Peak incidence: 3–6 months of age.
- Highest mortality rate in infants.

SIGNS AND SYMPTOMS

- Acute onset of fever, tachypnea, dyspnea, dry cough, and **progressive hypoxemia**.
- Chest x-ray—diffuse bilateral interstitial infiltrates or alveolar disease, may have characteristic "ground glass" appearance.

DIAGNOSIS

Diagnosis by **methenamine silver staining of bronchoalveolar lavage (BAL)** to identify cyst walls or Giemsa staining to identify nuclei of trophozoites. LDH > 500.

TREATMENT

- First-line treatment with prednisone is trimethoprim-sulfamethoxazole (TMP-SMX) (TMP: 15–20 mg/kg/24 hr; SMX: 75–100 mg/kg/24 hr) q6h for 5–7 days.
- Alternative regimens: Pentamidine, TMP-SMX plus dapsone, atovaquone.

PROPHYLAXIS

Starting at 6 weeks of age TMP-SMX if CD4 < 15%, or <200 for age 6–12 years and <500 for age 1–5 years. Risk displacement of bilirubin in neonate.

ATYPICAL MYCOBACTERIAL INFECTIONS

ETIOLOGY

- *Mycobacterium avium* complex (MAC).
- Considered an AIDS-defining illnesses. Patients with CD4 counts <50/mm^3 are at highest risk.

SIGNS AND SYMPTOMS

Disseminated disease:
- Fever.
- Malaise.
- Weight loss.
- Night sweats.
- May have gastrointestinal (GI) symptoms.

WARD TIP

Rifabutin ↓ serum levels of zidovudine (ZDV) and clarithromycin.

WARD TIP

Fluconazole can ↓ the level of rifabutin by 80%.

DIAGNOSIS

Diagnosis by culture from blood, bone marrow, or tissue.

TREATMENT

Two-drug regimen:
- Either clarithromycin *or* azithromycin.
- *Plus* ethambutol, rifabutin, rifampin, ciprofloxacin, *or* amikacin.

PROPHYLAXIS

For CD4 < 50: Azithromycin once a week.

CYTOMEGALOVIRUS (CMV)

ETIOLOGY

Member of Herpesvirus family.

PATHOPHYSIOLOGY

Infection is lifelong, as with any other herpesvirus. It may be acquired early in life and stay latent until the host becomes immunocompromised, years later. Lung, liver, kidney, GI tract, and salivary glands are the most common organs infected.

SIGNS AND SYMPTOMS

- Pneumonitis.
- Esophagitis.
- **Retinitis** (can cause blindness).

DIAGNOSIS

- Reactivation may be associated with appearance of IgM in serum.
- The pp65 antigen in white blood cells is used to detect infection in immunocompromised hosts. Quantitative polymerase chain reaction (PCR) as a measure of viral load in blood is available.
- Urine shedding of virus is lifelong. Positive urine CMV culture does not indicate association with current disease.

TREATMENT

- Gancyclovir. Systemic plus intraocular treatment for retinitis.
- IV foscarnet in gancyclovir-resistant infection.

Gastrointestinal Disease

Esophageal Atresia

A full-term infant was noted to have copious oral secretions requiring frequent suctioning to prevent choking. Attempts to place a nasogastric tube were unsuccessful, with the tube curling in the esophagus. X-ray is shown in the figure. What is the likely diagnosis and management of this condition?

The nasogastric tube with the tip in the proximal esophagus and failure to advance further signifies an esophageal atresia. The most common type is where the proximal esophagus ends in a blind pouch (as in this case) and there is a distal tracheoesophageal fistula. Also evident are ribs and vertebral anomalies in this case. This could be part of VATER (vertebral anomalies, anal atresia, tracheoesophageal anomalies, renal anomalies) syndrome. Infant was noted to have a single right kidney on renal ultrasound. Management includes surgical repair of the tracheoesophageal fistula.

DEFINITION

- The esophagus ends blindly ~10–12 cm from the nares.
- Occurs in 1/3000–1/4500 live births.
- In 85% of cases the distal esophagus communicates with the posterior trachea (distal tracheoesophageal fistula [TEF]).

SIGNS AND SYMPTOMS

- History of maternal polyhydramnios.
- Newborn with ↑ oral secretions.
- Choking, cyanosis, coughing during feeding (more commonly aspiration of pharyngeal secretions).
- Esophageal atresia with fistula.
- Aspiration of gastric contents via distal fistula—life threatening (chemical pneumonitis).
- Tympanitic distended abdomen.
- Esophageal atresia without fistula.
- Recurrent coughing with aspiration pneumonia (delayed diagnosis).
- Aspiration of pharyngeal secretions common.
- Airless abdomen on abdominal x-ray.

DIAGNOSIS

- Usually made at delivery.
- Unable to pass nasogastric tube (NGT) into stomach (see coiled NGT on chest x-ray).
- May also use contrast radiology, video esophagram, or bronchoscopy.
- Chest x-ray (CXR) demonstrates air in upper esophagus (see Figure 11-1).

TREATMENT

Surgical repair (may be done in stages).

F I G U R E 1 1 - 1 . Esophageal atresia. Radiograph demonstrating air in the upper esophagus (arrow) and GI tract, consistent with esophageal atresia.

Esophageal Foreign Body

- Most commonly due to swallowing of radiopaque objects: Coins, pins, pills, screws, and batteries.
- Preexisting abnormalities (i.e., tracheoesophageal repair) result in ↑ risk of having foreign body impaction at site of abnormality.
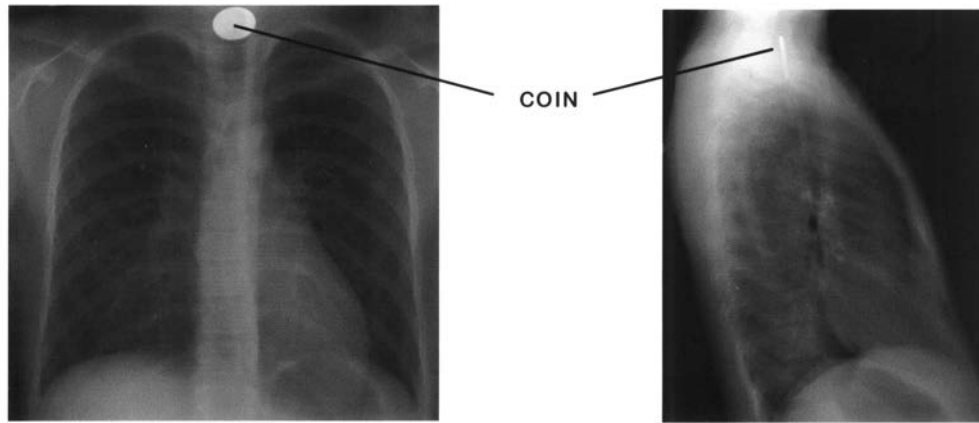
F I G U R E 1 1 - 2 . **Esophageal foreign body.** A coin in the esophagus will be seen flat or en face on an AP radiograph, and on its edge on a lateral view. (Used with permission from Dr. Julia Rosekrans.)

- Site of impaction:
  - 70%: Thoracic inlet (between clavicles on CXR).
  - 15%: Midesophagus.
  - 15%: Lower esophageal sphincter (LES).

SIGNS AND SYMPTOMS

- Gagging/choking.
- Difficulty with secretions.
- Dysphagia/food refusal.
- Throat pain or chest pain.
- Emesis/hematemesis.

DIAGNOSIS

- History, sometime witnessed event.
- X-ray (AP/lateral CXR; see Figure 11-2).

TREATMENT

- Objects found within the esophagus are generally considered impacted.
- Generally require endoscopic treatment if symptomatic or fail to pass to stomach (below diaphragm on x-ray) within a few hours.
- Impacted objects, pointed objects, and batteries must be removed immediately.
- Important to assess time of ingestion; >24 hours can → erosion or necrosis of esophageal wall.

> **WARD TIP**
>
> The most common site of esophageal impaction is at the thoracic inlet.

> **WARD TIP**
>
> Button batteries may rapidly cause local necrosis.

Gastroesophageal Reflux Disease (GERD)

An 8-month-old preterm infant has been hospitalized for 4 months in the neonatal care unit. In the past 2 weeks, the nurses have noted that he is regurgitating several times an hour. He makes chewing movements preceding these episodes of regurgitation. *Think: Rumination.*

Gastroesophageal reflux (GER) is common in preterm infants. Transient relaxation of the lower esophageal sphincter is the most common mechanism implicated. Signs and symptoms include apnea, chronic lung disease, poor weight gain, and behavioral symptoms. Frequent regurgitation and feeding difficulties may occur.

DEFINITION

- Passive reflux of gastric contents due to incompetent lower esophageal sphincter (LES).
- Approximately 1 in 300 children suffer from significant reflux and complication.
- Functional gastroesophageal reflux is most common.

RISK FACTORS

- Prematurity.
- Neurologic disorders.
- Incompetence of LES due to prematurity, asthma.
- Medications (theophylline, calcium channel blockers or β-blockers).

SIGNS AND SYMPTOMS

- Excessive spitting up in the first week of life (in 85% of affected).
- Symptomatic by 6 weeks (10%).
- Symptoms resolve without treatment by age 2 (60%).
- Forceful vomiting (occasional).
- Aspiration pneumonia (30%).
- Chronic cough, wheezing, and recurrent pneumonia (later childhood).
- Rarely may cause laryngospasm, apnea, and bradycardia.
- Regurgitation.

DIAGNOSIS

- Clinical assessment in mild cases.
- Esophageal pH probe studies and barium esophagography in severe cases.
- Esophagoscopy with biopsy for diagnosis of esophagitis.

TREATMENT

- Positioning following feeds—keep infant upright up to an hour after feeds.
- In older children, mealtime more than 2 hours before sleep and sleeping with head elevated.
- Thickening formula with rice cereal.
- Medications:
    - Antacids, histamine-2 (H_2) blockers (ranitidine), and proton pump inhibitors (PPIs; omeprazole).
    - Motility agents such as metoclopramide and erythromycin (stimulate gastric emptying).
    - Surgery—Nissen fundoplication.

> **WARD TIP**
>
> GERD is the etiology for Sandifer syndrome (reflux, back arching, stiffness, and torticollis). Sandifer syndrome is most often confused with a neurologic or apparent life-threatening event.

Peptic Ulcer

DEFINITION

Includes primary and secondary (related to stress).

SIGNS AND SYMPTOMS

- **Primary**—pain, vomiting, and acute and chronic gastrointestinal (GI) blood loss.
    - First month of life: GI hemorrhage and perforation.
    - Neonatal—2 months: Recurrent vomiting, slow growth, and GI hemorrhage.

- Preschool: Periumbilical and postprandial pain (with vomiting and hemorrhage).
- >6 years: Epigastric abdominal pain, acute/chronic GI blood loss with anemia.
- **Secondary:**
    - Stress ulcers secondary to sepsis, respiratory or cardiac insufficiency, trauma, or dehydration in infants.
    - Related to trauma or other life-threatening events (older children).
    - Stress ulcers and erosions associated with burns (Curling ulcers).
    - Ulcers following head trauma or surgery usually Cushing ulcers.
    - Drug related—nonsteroidal anti-inflammatory drugs (NSAIDs) or steroids.
    - Infectious—*Helicobacter pylori*.

DIAGNOSIS

- Upper GI endoscopy.
- Barium meal not sensitive.
- Plain x-rays may diagnose perforation of acute ulcers.
- Angiography can demonstrate bleeding site.
- *H. pylori* testing (hydrogen breath test, stool antigen).

TREATMENT

- Antibiotics for eradication of *H. pylori*: Triple therapy—PPI + 2 antibiotics (amoxicillin, clarithromycin, PPI).
- Antacids, sucralfate, and misoprostol.
- H_2 blockers and PPIs.
- Give prophylaxis for peptic ulcer when child is NPO or is receiving steroids.
- Endoscopic cautery.
- Surgery (vagotomy, pyloroplasty, or antrectomy) for extreme cases.

> **WARD TIP**
>
> Antimicrobials: 14 days
> PPIs: 1 month

Colic

DEFINITION

- Rule of 3's: Crying >3 hours/day, >3 days/week for >3 weeks between the ages of 3 weeks and 3 months.
- Frequent complex paroxysmal abdominal pain, severe crying.
- Usually in infants <3 months old.
- Etiology unknown. Can be related to under- or overfeeding, milk protein allergy, parental stress, and smoking.
- Colic is a diagnosis of exclusion. First look for other causes (hair in eye, corneal abrasion, strangulated hernia, otitis media, sepsis, etc.).

SIGNS AND SYMPTOMS

- Sudden-onset loud crying (paroxysms may persist for several hours).
- Facial flushing.
- Circumoral pallor.
- Distended, tense abdomen.
- Legs drawn up on abdomen.
- Feet often cold.
- Temporary relief apparent with passage of feces or flatus.

> **WARD TIP**
>
> A head-to-toe examination is essential. Physical examination MUST be normal.

TREATMENT

- No single treatment provides satisfactory relief.
- Careful exam is important to rule out other causes.
- Improve feeding techniques (burping).
- Avoid over- or underfeeding.
- Resolves spontaneously with time.

Pyloric Stenosis

A 4-week-old male infant has a 5-day history of vomiting after feedings. Physical exam shows a hungry infant with prominent peristaltic waves in the epigastrium. Laboratory evaluation revealed the following: Na 129, Cl 92, HCO_3 28, K 3.1, BUN 24. *Think: Hypertrophic pyloric stenosis.*

Pyloric stenosis is the most common cause of intestinal obstruction in infants. It is more common in males (M:F 4:1). It usually presents during the third to fifth week of life. Initial symptom is nonbilious vomiting. Classic sign of olive mass is not as common since increasing awareness has resulted in ultrasound imaging and early diagnosis. Criteria for diagnosis include pyloric muscle thickness >4 mm and length of pyloric canal >14 mm. Hypochloremic, hypokalemic metabolic alkalosis is the classic electrolyte abnormality.

DEFINITION

- Most common etiology is idiopathic.
- Not usually present at birth.
- Associated with exogenous administration of erythromycin, eosinophilic gastroenteritis, epidermolysis bullosa, trisomy 18, and Turner syndrome.
- First-born male.

SIGNS AND SYMPTOMS

- Typical: Projectile vomiting, palpable mass, and peristalsis—not always present.
- Nonbilious vomiting (projectile or not).
- Usually progressive, after feeding.
- Usually after 3 weeks of age, may be as late as 5 months.
- Hypochloremic, hypokalemic metabolic alkalosis (rare these days due to earlier diagnosis).
- Palpable pyloric olive-shaped mass in midepigastrium (difficult to find).
- Visible peristalsis: Left to right.

DIAGNOSIS

- Ultrasound (90% sensitivity).
- Elongated pyloric channel (>14 mm).
- Thickened pyloric wall (>4 mm).
- Radiographic contrast series (Figure 11-3).
- String sign: From elongated pyloric channel.
- Shoulder sign: Bulge of pyloric muscle into the antrum.
- Double tract sign: Parallel streaks of barium in the narrow channel.

TREATMENT

- Surgery: Pyloromyotomy is curative.
- Must correct existing dehydration and acid-base abnormalities prior to surgery.
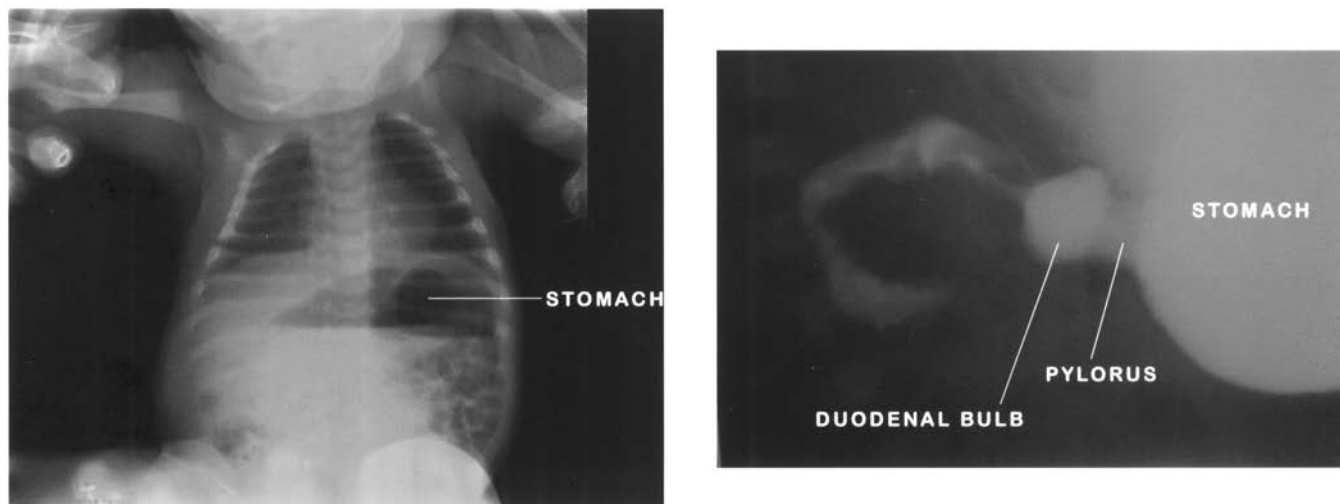
FIGURE 11-3. **Abdominal x-ray on the left demonstrates a dilated air-filled stomach with normal caliber bowel, consistent with gastric outlet obstruction.** Barium meal figure on the right confirms diagnosis of pyloric stenosis. The dilated duodenal bulb is the "olive" felt on physical exam. Note how there is a paucity of contrast traveling through the duodenum. (Used with permission from Drs. Julia Rosekrans and James E. Colletti.)

Duodenal Atresia

DEFINITION

- Failure to recanalize lumen after solid phase of intestinal development.
- Several forms.

SIGNS AND SYMPTOMS

- Bilious vomiting without abdominal distention (first day of life). Onset of vomiting within hours of birth.
- Can be nonbilious if the defect is proximal to the ampulla of Vater.
- Scaphoid abdomen.
- Placement of orogastric tube typically yields a significant amount of bile-stained fluid.
- History of polyhydramnios in 50% of pregnancies.
- Down syndrome seen in 20–30% of cases.
- Associated anomalies include malrotation, esophageal atresia, and congenital heart disease.

DIAGNOSIS

- Clinical.
- X-ray findings: Double-bubble sign (air bubbles in the stomach and duodenum) proximal to the site of atresia (Figure 11-4).

TREATMENT

- Initially, nasogastric and orogastric decompression with intravenous (IV) fluid replacement.
- Treat life-threatening anomalies.
- Surgery.
- Duodenoduodenostomy.
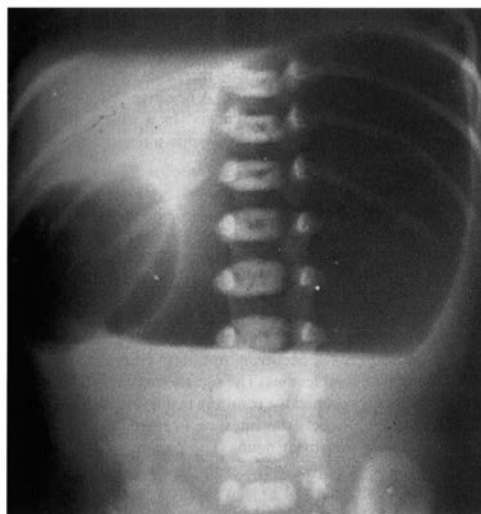
F I G U R E 1 1 - 4 .   **Duodenal atresia.** Gas-filled and dilated stomach shows the classic "double-bubble" appearance of duodenal atresia. Note no distal gas is present. (Reproduced, with permission, from Rudolph CD, et al (eds). *Rudolph's Pediatrics*, 21st ed. New York: McGraw-Hill, 2002: 1403.)
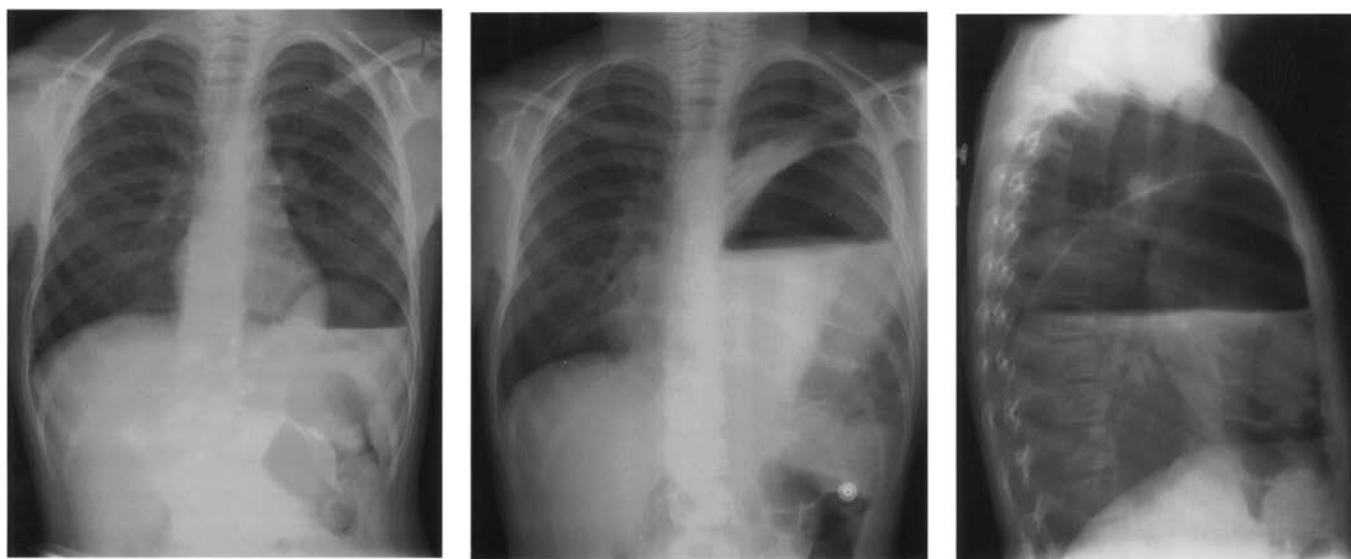
F I G U R E 1 1 - 5 .   **Volvulus.** First AP view done 6 weeks prior to the second AP and corresponding lateral view. Note the markedly dilated stomach above the normal level of the left hemidiaphragm in the thoracic cavity. Also present is a large left-sided diaphragmatic hernia. (Used with permission from Dr. Julia Rosekrans.)

Volvulus

DEFINITION

- Gastric and intestinal:
  - Gastric: Sudden onset of severe epigastric pain; intractable retching with emesis.
  - Intestinal: Associated with malrotation (Figure 11-5).
- Volvulus occurs as a consequence of intestinal malrotation—obstruction is complete, and compromise to the blood supply of the midgut has started.

RISK FACTORS

- Embryological abnormalities: Arrest of development at any stage during embryological development of GI tract can → changes in anatomical position of organs and narrowing of mesenteric base, resulting in ↑ risk for volvulus.
- Male-to-female presentation: 2:1.

SIGNS AND SYMPTOMS

- Vomiting in infancy.
- Emesis (commonly bilious).
- Abdominal pain → acute abdomen.
- Early satiety.
- Blood-stained stools.
- Distention.
- A neonate with bilious vomiting must be considered at risk for having a midgut volvulus.

DIAGNOSIS

- Plain abdominal films: Characteristic bird-beak appearance.
- May also see air-fluid level without beak.

TREATMENT

- Treatment is surgical correction.
- Gastric: Emergent surgery.
- Intestinal: Surgery or endoscopy.

COMPLICATIONS

- Perforation.
- Peritonitis.

Intussusception

A 9-month-old female infant was brought to the ED due to vomiting and crying. She had a "cold" 3 days ago. On arrival she was sleepy but arousable. When she woke up, she cried and vomited. Physical examination revealed distended abdomen with an ill-defined mass in the right upper abdomen. What is the cause of her symptoms? Intussusception.

How she should be treated? A contrast enema should be performed to reduce the intussusception. It is both diagnostic and therapeutic. It should be performed in consultation with a pediatric surgeon caring for the child and a pediatric radiologist interpreting the study. It is the most common cause of intestinal obstruction between 5 months and 6 years of age. Most children with intussusception are under 1 year of age. The classic triad of intermittent, colicky abdominal pain; vomiting; and bloody, mucous stools occur in only 20–40%.

DEFINITION

Invagination of one portion of the bowel into itself. The proximal portion is usually drawn into the distal portion by peristalsis.

EPIDEMIOLOGY

- Incidence: 1–4 in 1000 live births.
- Male-to-female ratio: 2:1 to 4:1.

- Peak incidence: 5–12 months.
- Age range: 2 months to 5 years.
- Most common cause of acute intestinal obstruction under 2 years of age.
- Most common site is ileocolic (90%).

ETIOLOGY

- Most common etiology is idiopathic.
- Other causes:
    - Viral (enterovirus in summer, rotavirus in winter).
    - A "lead point" (or focus) is thought to be present in older children 2–10% of the time. These lead points can be caused by Meckel's diverticulum, polyp, lymphoma, Henoch-Schönlein purpura, cystic fibrosis.

SIGNS AND SYMPTOMS

- Classic triad:
    - Intermittent colicky abdominal pain.
    - Bilious vomiting.
    - Currant jelly stool (late finding).
- Neurologic signs:
    - Lethargy
    - Shocklike state.
    - Seizure activity.
    - Apnea.
- Right upper quadrant mass:
    - Sausage shaped.
    - Ill defined.
    - Dance's sign: Absence of bowel in right lower quadrant.

DIAGNOSIS

- Abdominal x-ray:
    - X-ray is neither specific nor sensitive. Can be completely normal.
    - Paucity of bowel gas (Figure 11-6).

FIGURE 11-6.   Intussusception. Note the paucity of bowel gas in film **(A)** Air enema partially reduces it in film **(B)** and then completely reduced it in film **(C)**.

- Loss of visualization of the tip of liver.
- "Target sign": Two concentric circles of fat density.
- Ultrasound:
  - Test of choice.
  - "Target" or "donut" sign: Single hypoechoic ring with hyperechoic center.
  - "Pseudokidney" sign: Superimposed hypoechoic (edematous walls of bowel) and hyperechoic (areas of compressed mucosa) layers.
- Barium enema:
  - Not useful for ileoileal intussusceptions.
  - May note cervix-like mass.
  - Coiled spring appearance on the evacuation film.
  - Contraindications: Peritonitis, perforation, profound shock/hemodynamic instability.
- Air enema:
  - Air enema is preferred (safe, with a lower absorbed radiation).
  - Often provides the same diagnostic and therapeutic benefit of a barium enema without the barium.

TREATMENT

- Correct dehydration.
- NG tube for decompression.
- Hydrostatic reduction.
- Barium/air enema (see Figure 11-7).
- Surgical reduction:
  - Failed reduction by enema.
  - Clinical signs of perforation or peritonitis.
- Recurrence:
  - With radiologic reduction: 7–10%.
  - With surgical reduction: 2–5%.

> **WARD TIP**
>
> Contrast enema for intussusception can be both diagnostic and therapeutic. Rule of threes:
> - Barium column should not exceed a height of 3 feet.
> - No more than 3 attempts.
> - Only 3 minutes/attempt.

FIGURE 11-7. Abdominal x-ray following barium enema in a 2-month-old boy, consistent with intussusception. Note paucity of gas in right upper quadrant and near obscuring of liver tip.

Meckel's Diverticulum

DEFINITION

Persistence of the omphalomesenteric (vitelline) duct (should disappear by seventh week of gestation).

SIGNS AND SYMPTOMS

- Usually in first 2 years:
    - Intermittent painless rectal bleeding (hematochezia—most common presenting sign).
    - Intestinal obstruction.
    - Diverticulitis.
- Occurs on the antimesenteric border of the ileum, usually 40–60 cm proximal to the ileocecal valve.

DIAGNOSIS

- Meckel's scan (scintigraphy) has 85% sensitivity and 95% specificity. Uptake can be enhanced with cimetidine, glucagons, or gastrin.
- Most common heterotopic mucosa is gastric.

TREATMENT

Surgical: Diverticular resection with transverse closure of the enterotomy.

Appendicitis

DEFINITION

- Acute inflammation and infection of the vermiform appendix.
- Most common cause for emergent surgery in childhood.
- Perforation rates are greatest in youngest children (can't localize symptoms).
- Occurs secondary to obstruction of lumen of appendix.
- Three phases:
    1. Luminal obstruction, venous congestion progresses to mucosal ischemia, necrosis, and ulceration.
    2. Bacterial invasion with inflammatory infiltrate through all layers.
    3. Necrosis of wall results in perforation and contamination.

SIGNS AND SYMPTOMS

- Classically: Pain, vomiting, and fever.
- Initially, periumbilical pain; emesis infrequent.
- Anorexia.
- Low-grade fever.
- Diarrhea infrequent.
- Pain radiates to right lower quadrant.
- Perforation rate >65% after 48 hours.
- Rectal exam may reveal localized mass or tenderness.

DIAGNOSIS

- History and physical exam is key to rule out alternatives first.
- Pain usually occurs before vomiting, diarrhea, or anorexia.
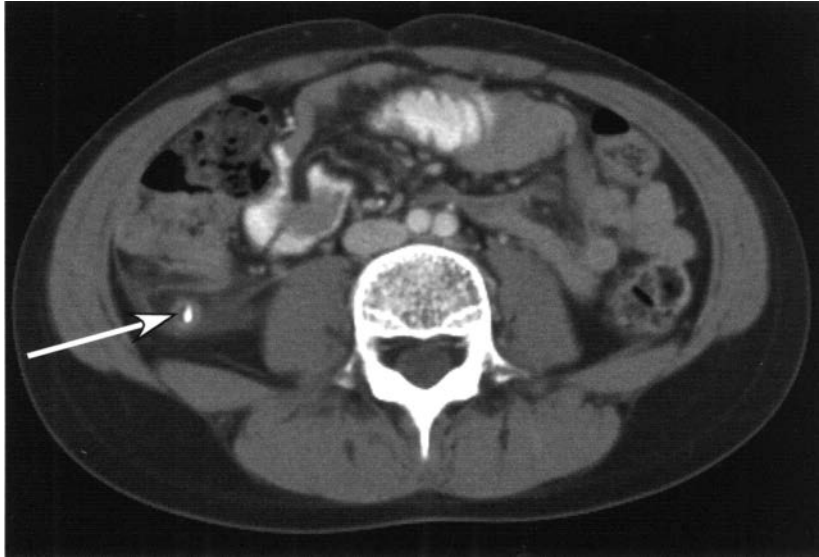
FIGURE 11-8.   **Abdominal CT of a 10-year-old girl demonstrating enlargement of the appendix, some periappendiceal fluid, and an appendicolith (arrow), consistent with acute appendicitis.**

- Atypical presentations are common—risk for misdiagnosis.
- Most common misdiagnosis: Gastroenteritis.
- Labs helpful to rule other diagnosis but no laboratory test specific for appendicitis.
- Computed tomographic (CT) scan (Figure 11-8) indicated for patients in whom diagnosis is equivocal—not a requirement for all patients.
- Higher rate of ruptured appendix on presentation in young children.

TREATMENT

- Surgery as soon as diagnosis made.
- Antibiotics are controversial in nonperforated appendicitis.
- Broad-spectrum antibiotics needed for cases of perforation (ampicillin, gentamicin, clindamycin, or metronidazole × 7 days).
- Laparoscopic removal associated with shortened hospital stay (nonperforated appendicitis).

Constipation

A 4-year-old girl has not had a bowel movement for a week, and this has been a recurring problem. Various laxatives and enemas have been tried in the past. Prior to toilet training, the girl had one bowel movement a day. Physical examination is normal except for the presence of stool in the sigmoid colon and hard stool on rectal examination. After removing the impaction, the next appropriate step in management would be to administer mineral oil or other stool softener.

Constipation is a common problem in children. It is the most common cause of abdominal pain in children. Functional constipation is more common in children, and organic causes are common in neonates. The physical examination often reveals a large volume of stool palpated in the suprapubic region. The finding of rectal impaction may establish the diagnosis.

DEFINITION/SIGNS AND SYMPTOMS

- Common cause of abdominal pain in children.
- Passage of bulky or hard stool at infrequent intervals.
- During the neonatal period usually caused by Hirschsprung, intestinal pseudo-obstruction, or hypothyroidism.
- Other causes include organic and inorganic (e.g., cow's milk protein intolerance, drugs).
- May be metabolic (dehydration, hypothyroidism, hypokalemia, hypercalcemia, psychiatric).

TREATMENT

- ↑ oral fluid and fiber intake.
- Stool softeners (e.g., mineral oil).
- Glycerin suppositories.
- Cathartics such as senna or docusate.
- Nonabsorbable osmotic agents (polyethylene glycol) and milk of magnesia for short periods only if necessary—can cause electrolyte imbalances.

Hirschsprung's Megacolon

A full-term male infant was noted to have progressive abdominal distention on the second day of life, with no stool since birth. He was feeding well on demand whether mother's milk or infant formula. He was otherwise healthy, active, and had no signs of infection. Abdominal x-ray is consistent with distended loops of bowel with no evidence of free air. Contrast enema is notable for a narrowed segment of the colon leading to a very distended loop.

The diagnosis is likely Hirschsprung disease. Hirschsprung disease results from absence of ganglion cells in the bowel wall and resultant narrowed segment of the bowel. The proximal normal bowel progressively dilates due to accumulated food. Definitive diagnosis is made by rectal biopsy, which demonstrates absent ganglion cells.

DEFINITION

- Abnormal innervation of bowel (i.e., absence of ganglion cells in bowel).
- ↑ in familial incidence.
- Occurs in males more than females.
- Associated with Down syndrome.

SIGNS AND SYMPTOMS

- Delayed passage of meconium at birth.
- ↑ abdominal distention → ↓ blood flow → deterioration of mucosal barrier → bacterial proliferation → enterocolitis.
- Chronic constipation and abdominal distention (older children).

DIAGNOSIS

- Rectal manometry: Measures pressure of the anal sphincter.
- Rectal suction biopsy: Must obtain submucosa to evaluate for ganglionic cells.

TREATMENT

Surgery is definitive (usually staged procedures).

Imperforate Anus

DEFINITION

- Absence of normal anal opening.
- Rectum is blind; located 2 cm from perineal skin.
- Sacrum and sphincter mechanism well developed.
- Prognosis good.
- Can be associated with VACTERL anomalies.

SIGNS AND SYMPTOMS

- First newborn examination in nursery.
- Failure to pass meconium.
- Abdominal distention.

DIAGNOSIS

- Physical examination.
- Abdominal ultrasonography to examine the genitourinary tract.
- Sacral radiography.
- Spinal ultrasound: Association with spinal cord abnormalities, particularly spinal cord tethering.

TREATMENT

Surgery (colostomy in newborn period).

> **WARD TIP**
>
> Imperforate anus is frequently associated with Down syndrome and VACTERL.

Anal Fissure

> A well-nourished 3-month-old infant is brought to the ED because of constipation, blood-streaked stools, and excessive crying on defecation. *Think: Anal fissure.*
> Anal fissure is a painful linear tear or crack in the distal anal canal. Constipation may be exacerbated because of fear of pain with defecation. Diagnosis often can be made based on history and physical examination.

DEFINITION

- Painful linear tears in the anal mucosa below the dentate line induced by constipation or excessive diarrhea.
- Tear of squamous epithelium of anal canal between anocutaneous junction and dentate line.
- Often history of constipation is present.
- Predilection for the posterior midline.
- Common age: 6–24 months.

SIGNS AND SYMPTOMS

- Pain with defecation/crying during bowel movement.
- ↑ sphincter tone.
- Visible tear upon gentle lateral retraction of anal tissue.

DIAGNOSIS

Anal inspection.

TREATMENT

Sitz baths, fiber supplements, ↑ fluid intake.

TABLE 11-1. Crohn Disease versus Ulcerative Colitis

FEATURE	CROHN DISEASE	ULCERATIVE COLITIS (UC)
Depth of involvement	Transmural	Mucosal
Ileal involvement	Common	Unusual
Ulcers	Common	Unusual
Cancer risk	↓	↑
Pyoderma gangrenosum	Slightly ↑	Greatly ↑
Skip lesions	Common	Unusual
Fistula	Common	Unusual
Rectal bleeding	Sometimes	Common

Inflammatory Bowel Disease

DEFINITION

Idiopathic chronic diseases include Crohn disease and ulcerative colitis (UC).

EPIDEMIOLOGY

- Common onset in adolescence and young adulthood.
- Bimodal pattern in patients 15–25 and 50–80 years of age.
- Genetics: ↑ concordance with monozygotic twins versus dizygotic (↑ for Crohn versus UC).

SIGNS AND SYMPTOMS (TABLE 11-1)

- Crampy abdominal pain.
- Extraintestinal manifestations greater in Crohn than UC.
- Crohn: Perianal fistula, sclerosing cholangitis, chronic active hepatitis, pyoderma gangrenosum, ankylosing spondylitis, erythema nodosum.
- UC: Bloody diarrhea, anorexia, weight loss, pyoderma gangrenosum, sclerosing cholangitis, marked by flare-ups.

TREATMENT

- Crohn disease: Corticosteroids, aminosalicylates, methotrexate, azathioprine, cyclosporine, metronidazole (for perianal disease), sitz baths, anti–tumor necrosis factor-α, surgery for complications.
- UC: Aminosalicylates, oral corticosteroids, colectomy.

Irritable Bowel Syndrome

DEFINITION

Abdominal pain associated with intermittent diarrhea and constipation without organic basis; ~10% in adolescents.

SIGNS AND SYMPTOMS

- Abdominal pain.
- Diarrhea alternating with constipation.

DIAGNOSIS

- Difficult to make, exclude other pathology.
- Obtain CBC, ESR, stool occult blood.

TREATMENT

- None specific.
- Supportive with reinforcement and reassurance.
- Address any underlying psychosocial stressors.

Acute Gastroenteritis and Diarrhea

DEFINITION

- **Diarrhea** is the excessive loss of fluid and electrolytes in stool, usually secondary to disturbed intestinal solute transport. Technically limited to lower GI tract.
- **Gastroenteritis** is an inflammation of the entire (upper and lower) GI tract, and thus involves both vomiting and diarrhea.

EPIDEMIOLOGY

- ↑ susceptibility seen in young age, immunodeficiency, malnutrition, travel, lack of breast-feeding, and contaminated food or water.
- Most common cause of diarrhea in children is viral: (1) rotavirus, (2) enteric adenovirus, (3) Norwalk virus.
- Bacterial: (1) *Campylobacter*, (2) *Salmonella* and *Shigella* species and enterohemorrhagic *Escherichia coli*.
- Children in developing countries often also get infected by bacterial and parasitic pathogens:
  - Enterotoxigenic *E. coli* number one in developing countries.
  - Parasitic causes: (1) *Giardia* and (2) *Cryptosporidium*.

SIGNS AND SYMPTOMS

- Important to obtain information regarding frequency and volume.
- General patient appearance important (well appearing versus ill appearing).
- Associated findings include cramps, emesis, malaise, and fever.
- May see systemic manifestations, GI tract involvement, or extraintestinal infections.
- Extraintestinal findings include vulvovaginitis, urinary tract infection (UTI), and keratoconjunctivitis.
- Systemic manifestations: Fever, malaise, and seizures.
- Inflammatory diarrhea: Fever, severe abdominal pain, tenesmus. May have blood/mucus in stool.
- Noninflammatory diarrhea: Emesis, fever usually absent, crampy abdominal pain, watery diarrhea.

DIAGNOSIS

- Examine stool for mucus, blood, and leukocytes (colitis).
- Fecal leukocyte: Presence of invasive cytotoxin organisms (*Shigella*, *Salmonella*).

WARD TIP

Acute diarrhea is usually caused by infectious agents, whereas chronic persistent diarrhea may be secondary to infectious agents, infection of immunocompromised host, or residual symptoms due to intestinal damage.

WARD TIP

- Diarrhea and emesis—noninflammatory
- Diarrhea and fever—inflammatory process
- Diarrhea and tenesmus—large colon involvement

- Patients with enterohemorrhagic *E. coli* and *Entamoeba histolytica:* Minimal to no fecal leukocytes.
- Obtain stool cultures early.
- *Clostridium difficile* toxins: Test if recent antibiotic use.
- Proctosigmoidoscopy: Diagnosis of inflammatory enteritis.

TREATMENT

- Rehydration.
- Oral electrolyte solutions (e.g., Pedialyte®).
- Oral hydration for all but severely dehydrated (IV hydration).
- Rapid rehydration with replacement of ongoing losses during first 4–6 hours.
- Do not use soda, fruit juices, gelatin, or tea. High osmolality may exacerbate diarrhea.
- Start food with BRAT diet.
- Antidiarrheal compounds are not indicated for use in children.
- See Table 11-2 for antibiotic treatment of enteropathogens (wait for diagnosis via stool culture, empiric antibiotics generally not indicated).

PREVENTION

- Hospitalized patients should be placed under contact precautions (hand washing, gloves, gowns, etc.).
- Education.
- Exclude infected children from child care centers.
- Report cases of bacterial diarrhea to local health department.
- Vaccines for cholera and *Salmonella typhi* are available.

TABLE 11-2. **Antimicrobial Treatment for Bacterial Enteropathogens**

BACTERIA	TREATMENT	COMMENTS
Aeromonas	Trimethoprim-sulfamethoxazole (TMP-SMZ)	Prolonged diarrhea
Campylobacter	Erythromycin	Early in course of illness
Clostridium difficile	Metronidazole or vancomycin	Moderate to severe diagnosis
Escherichia coli		
Enterotoxigenic	TMP-SMZ	Severe or prolonged illness
Enteropathogenic	TMP-SMZ	Nursery epidemics
Enteroinvasive	TMP-SMZ	All cases
Salmonella	Ampicillin or chloramphenicol or TMP-SMZ	Infants < 3 months, immunodeficient patients, bacteremia
Shigella	TMP-SMZ, ceftriaxone	All susceptible organisms
Vibrio cholerae	Tetracycline or doxycycline	All cases

TABLE 11-3. **Common Intestinal Worms**

Intestinal Nematodes	Mode of Transmission	Disease, Symptoms and Signs	Treatment
Enterobius vermicularis (pinworm)	Hand to mouth	Perianal itching, especially at night	Albendazole or mebendazole or pyrantel pamoate 11 mg/kg (max. dose, 1 g PO × 1)
Trichuris trichuria (whipworm)	Fecal-oral	■ Usually asymptomatic ■ Mild anemia ■ Abdominal pain ■ Diarrhea, tenesmus ■ Perianal itching	Albendazole or mebendazole
Ascaris lumbricoides	Fecal-oral	■ Pneumonia ■ Loeffler pneumonitis ■ Intestinal infection/obstruction ■ Liver failure	Albendazole or mebendazole
Necator americanus (New World hookworm) and *Ancylostoma duodenale* (Old World hookworm)	Skin penetration	■ Intense dermatitis ■ Loeffler pneumonitis ■ Significant anemia ■ GI symptoms ■ Developmental delay in children (irreversible)	Albendazole or mebendazole
Strongyloides stercoralis	Skin penetration	Same as for *Necator,* plus: ■ Diarrhea × 3–6 weeks ■ Superimposed bacterial sepsis	Ivermectin 200 µg/kg/day × 2 days
Trichinella spiralis	Infected pork	Trichinosis ■ Myalgias ■ Facial and periorbital edema ■ Conjunctivitis ■ Pneumonia, myocarditis, encephalitis, nephritis, meningitis	Albendazole 400 mg PO bid × 14 days + prednisone 40–60 mg PO qd

Usual albendazole dose is 400 mg PO × 1; usual mebendazole dose is 100 mg PO × 1 for 3 days.

(Adapted, with permission, from Stead L. BRS Emergency Medicine. Lippincott Williams & Wilkins, 2000.)

Intestinal Worms

See Table 11-3 for common intestinal worm infestations.

Pseudomembranous Colitis

DEFINITION

■ Major cause of iatrogenic diarrhea.
■ Rarely occurs without antecedent antibiotics (usually) penicillins, cephalosporins, or clindamycin.

- Antibiotic disrupts normal bowel flora and predisposes to *C. difficile* diarrhea.
- Stool should be tested for *C. difficile* toxins if there is a recent history of antibiotic use.

SIGNS AND SYMPTOMS

Classically, blood and mucus with fever, cramps, abdominal pain, nausea, and vomiting days or weeks after antibiotics.

DIAGNOSIS

- Recent history of antibiotic use.
- *C. difficile* toxin in stool of patient with diarrhea.
- Sigmoidoscopy or colonoscopy.

TREATMENT

- Discontinue antibiotics.
- Oral metronidazole or vancomycin × 7–10 days.

Abdominal Hernias

UMBILICAL

DEFINITION

- Occurs because of imperfect closure of umbilical ring.
- Common in low-birth-weight, female, and African-American infants.
- Soft swelling covered by skin that protrudes while crying, straining, or coughing.
- Omentum or portions of small intestine involved.
- Usually 1–5 cm.

TREATMENT

- Most disappear spontaneously by 1 year of age.
- Strangulation rare.
- "Strapping" ineffective.
- Surgery not indicated unless symptomatic, strangulated, or grows larger after age 1 or 2.

INGUINAL

DEFINITION

- Most common diagnosis requiring surgery.
- Occurs in 10–20/1,000 live births (50% <1 year).
- Indirect > direct (rare) > femoral (even more rare).
- Indirect secondary to patent processus vaginalis.
- ↑ incidence with positive family history.
- Embryology: Patent processus vaginalis.
- Incidence: 1–5%.
- Males > females 8–10:1.
- Preemies: 20% males, 2% females.
- Premature infants have ↑ risk for inguinal hernia.
- Sixty percent right (delayed descent of the right testicle), 30% left, 10% bilateral.
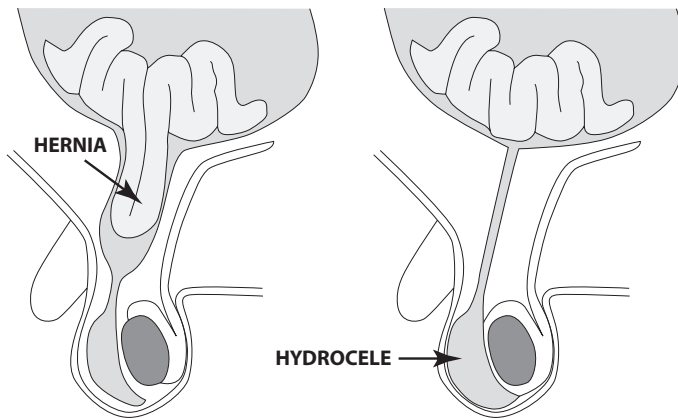
F I G U R E   1 1 - 9 . **Inguinal hernia (slippage of bowel through inguinal ring) vs. hydrocele (collection of fluid in scrotum adjacent to testes).**

SIGNS AND SYMPTOMS

- Infant with scrotal/inguinal bulge on straining or crying.
- Do careful exam to distinguish from hydrocele (see Figure 11-9).
- Bulge in groin ± scrotum, incarceration.

TREATMENT

- Surgery (elective).
- Avoid trusses or supports.
- Contralateral hernia occurs in 30% after unilateral repair.
- Antibiotics only in at-risk children (e.g., congenital heart disease).
- Prognosis excellent (recurrence <1%, complication rate approximately 2%, infection approximately 1%).
- Complications include incarceration.
- Therapy: Incarceration—sedation and manipulation 90–95% reduced. Immediate operation if not reduced. Repair soon after diagnosis especially infants since 60% progress to incarceration by 6 months.

> **WARD TIP**
>
> Inguinal hernia ↑ with straining; hydrocele remains unchanged.

Peutz-Jeghers Syndrome

> A 15-year-old girl with spots on her lips has some crampy abdominal pain associated with bleeding. *Think: Peutz-Jeghers syndrome.*
>
> Peutz-Jeghers syndrome is multiple GI hamartomatous polyps + mucocutaneous hyperpigmentation. There is a higher risk of intestinal and extraintestinal malignancies.

DEFINITION

- Mucosal pigmentation of lips and gums with hamartomas of stomach, small intestine, and colon.
- Rare; low malignant potential.

SIGNS AND SYMPTOMS

- Deeply pigmented freckles on lips and buccal mucosa at birth.
- Bleeding and crampy abdominal pain.

DIAGNOSIS

Genetic and family studies may reveal history.

TREATMENT

Excise intestinal lesions if significantly symptomatic.

Gardner Syndrome

DEFINITION

Multiple intestinal polyps, tumors of soft tissue and bone (especially mandible).

SIGNS AND SYMPTOMS

- Dental abnormalities.
- Pigmented lesions in ocular fundus.
- Intestinal polyps (usually early adulthood) with high malignant potential.

DIAGNOSIS

- Genetic counseling.
- Colon surveillance in at-risk children.

TREATMENT

Aggressive surgical removal of polyps.

Carcinoid Tumors

DEFINITION

Tumors of enterochromaffin cells in intestine—usually appendix.

SIGNS AND SYMPTOMS

- May cause appendicitis.
- May cause carcinoid syndrome (↑ serotonin, vasomotor disturbances, or bronchoconstriction) if metastatic to the liver.

TREATMENT

Surgical excision.

Familial Polyposis Coli

DEFINITION/ETIOLOGY

- Autosomal dominant.
- Large number of adenomatous lesions in colon.
- Secondary to germ-line mutations in adenopolyposis coli (APC) gene.

SIGNS AND SYMPTOMS

- Highly variable.
- May see hematochezia, cramps, or diarrhea.
- Extracolonic manifestations possible.

DIAGNOSIS

- Consider family history (strong).
- Colonoscopy with biopsy (screening annually after 10 years old if positive family history).

TREATMENT

Surgical resection of affected colonic mucosa.

Juvenile Polyposis Coli

DEFINITION

- Most common childhood bowel tumor (3–4% of patients <21 years).
- Characteristically, mucus-filled cystic glands (no adenomatous changes, no potential for malignancy).

EPIDEMIOLOGY

Most commonly between 2 and 10 years; less common after 15 years; rarely before 1 year.

SIGNS AND SYMPTOMS

- Bright-red painless bleeding with bowel movement.
- Iron deficiency.

DIAGNOSIS

- Colonoscopy.
- May use barium enema (not best test).

TREATMENT

Surgical removal of polyp.

Malabsorption

SHORT BOWEL SYNDROME

DEFINITION

- Occurs with loss of at least 50% of small bowel (with or without loss of large bowel).
- ↓ absorptive surface and bowel function.

ETIOLOGY

- May be congenital (malrotation, atresia, etc.).
- Most commonly secondary to surgical resection.

SIGNS AND SYMPTOMS

- Malabsorption and diarrhea.
- Steatorrhea (fatty stools): Voluminous foul-smelling stools that float.
- Dehydration.
- ↓ sodium and potassium.
- Acidosis (secondary to loss of bicarbonate).

TREATMENT

- Total parenteral nutrition (TPN).
- Give small feeds orally.
- Metronidazole empirically to treat bacterial overgrowth.

CELIAC DISEASE

> 👤 A 5-year-old girl presents with a protuberant abdomen and wasted extremities. *Think: Gluten-induced enteropathy.*
>
> Celiac disease is an autoimmune disorder. The disease primarily affects the small intestine. Gluten is the single major factor that triggers celiac disease. *Gluten-containing foods include* rye, wheat, and barley. Common presentation: diarrhea, borborygmus, abdominal pain, and weight loss. Other systems, including skin, liver, nervous system, bones, reproductive system, and endocrine system, may also be affected. *Serologic marker:* Serum immunoglobulin A (IgA) endomysial antibodies and IgA tissue transglutaminase (tTG) antibodies.

DEFINITION

- Sensitivity to gluten in diet.
- Most commonly occurs between 6 months and 2 years.

ETIOLOGY

- Factors involved include cereals, genetic predisposition, and environmental factors.
- Associated with HLA-B8, -DR7, -DR3, and -DQW2.

SIGNS AND SYMPTOMS

- Diarrhea.
- Failure to thrive.
- Vomiting.
- Pallor.
- Abdominal distention.
- Large bulky stools.

DIAGNOSIS

- Anti-endomysial and anti-tissue transglutaminase antibodies (check total lgH level at the same time).
- Biopsy: Most reliable test.

TREATMENT

- Dietary restriction of gluten (**must** avoid barley, ryes, oats, and wheat).
- Corticosteroids used rarely (very ill patients with profound malnutrition, diarrhea, edema, and hypokalemia).

TROPICAL SPRUE

DEFINITION

- Generalized malabsorption associated with diffuse lesions of small bowel mucosa.
- Seen in people who live or have traveled to certain tropical regions—some Caribbean countries, South America, Africa, or parts of Asia.

Signs and Symptoms

- Fever, malaise, and watery diarrhea, acutely.
- After 1 week, chronic malabsorption and signs of malnutrition including night blindness, glossitis, stomatitis, cheilosis, muscle wasting.

Diagnosis

Biopsy shows villous shortening, ↑ crypt depth, and ↑ chronic inflammatory cells in lamina propria of small bowel.

Treatment

- Antibiotics × 3–4 weeks.
- Folate.
- Vitamin B_{12}.
- Prognosis excellent.

LACTASE DEFICIENCY

Definition

↓ or absent enzyme that breaks down lactose in the intestinal brush border.

Etiology

- Congenital absence reported in few cases.
- Usual mechanism relates to developmental pattern of lactase activity.
- Autosomal recessive.
- Also ↓ because of diffuse mucosal disease (can occur post viral gastroenteritis).

Signs and Symptoms

- Seen in response to ingestion of lactose (found in dairy products).
- Explosive watery diarrhea with abdominal distention, borborygmi, and flatulence.
- Recurrent, vague abdominal pain.
- Episodic midabdominal pain (may or may not be related to milk intake).

Treatment

- Eliminate milk from diet.
- Oral lactase supplement (Lactaid) or lactose-free milk.
- Yogurt (with lactase enzyme–producing bacteria tolerable in such patients).

Hyperbilirubinemia

Physiology: See Gestation and Birth chapter.

Definition

Elevated serum bilirubin.

Epidemiology

- Common and in most cases benign.
- If untreated, severe indirect hyperbilirubinemia neurotoxic (kernic-terus).
- Jaundice in first week of life in 60% of term and 80% of preterm infants—results from accumulation of unconjugated bilirubin pigment.

SIGNS AND SYMPTOMS

- Jaundice at birth or in neonatal period.
- May be lethargic and feed poorly.

DIAGNOSIS

- Direct and indirect bilirubin fractions.
- Hemoglobin.
- Reticulocyte count.
- Blood type.
- Examine peripheral smear.

TREATMENT

- Goal is to prevent neurotoxic range.
- Phototherapy.
- Exchange transfusion.
- Treat underlying cause.

GILBERT SYNDROME

Benign condition caused by missense mutation in transferase gene resulting in low enzyme levels with unconjugated hyperbilirubinemia.

CRIGLER-NAJJAR I SYNDROME

DEFINITION

- Autosomal recessive, secondary to mutations in glucuronyl transferase gene.
- Parents of affected children show partial defects but normal serum bilirubin concentration.
- Complete absence of the enzyme uridine diphosphate glycosyltransferase.
- Much rarer than Gilbert syndrome.

SIGNS AND SYMPTOMS

- In homozygous infants, will see unconjugated hyperbilirubinemia in first 3 days of life.
- Kernicterus common in early neonatal period.
- Some treated infants survive childhood without sequelae.
- Stools pale yellow.
- Persistence of ↑ levels of indirect bilirubin after first week of life in absence of hemolysis suggests this syndrome.

DIAGNOSIS

- Based on early age of onset and extreme level of bilirubin in absence of hemolysis.
- Definitive diagnosis made by measuring glucuronyl transferase activity in liver biopsy specimen.
- DNA diagnosis available.

TREATMENT

- Maintain serum bilirubin <20 mg/dL for first 2–4 weeks of life.
- Repeated exchange transfusion.
- Phototherapy.
- Treat intercurrent infections.
- Hepatic transplant.

CRIGLER-NAJJAR II SYNDROME

DEFINITION

- Autosomal dominant with variable penetrance.
- May be caused by homozygous mutation in glucuronyl transferase isoform I activity.
- ↓ enzyme uridine diphosphate glycosyltransferase.

SIGNS AND SYMPTOMS

- Unconjugated hyperbilirubinemia in first 3 days of life.
- Concentration remains ↑ after third week of life.
- Kernicterus unusual.
- Stool normal.
- Infants asymptomatic.

DIAGNOSIS

- Concentration of bilirubin nearly normal.
- ↓ bilirubin after 7- to 10-day treatment with phenobarbital may be diagnostic.

TREATMENT

Phenobarbital for 7–10 days.

ALAGILLE SYNDROME

DEFINITION

- Absence or reduction in number of bile ducts.
- Results from progressive destruction of the ducts.

SIGNS AND SYMPTOMS

- Variably expressed.
- Unusual facies (broad forehead, wide-set eyes, underdeveloped mandible).
- Ocular abnormalities.
- Cardiovascular abnormalities (peripheral pulmonic stenosis).
- Tubulointerstitial nephropathy.
- Vertebral defect.

PROGNOSIS

Long-term survival good but may have pruritis, xanthomas, and ↑ cholesterol and neurologic complications.

ZELLWEGER SYNDROME

DEFINITION

- Rare autosomal-recessive condition causing progressive degeneration of liver and kidneys.
- Occurs in 1 in 100,000 births.

SIGNS AND SYMPTOMS

- Usually fatal within 6–12 months.
- Severe generalized hypotonia.
- Impaired neurologic function with psychomotor retardation.
- Abnormal head and unusual facies.

- Hepatomegaly.
- Renal cortical cysts.
- Ocular abnormalities.
- Congenital diaphragmatic hernia.

DIAGNOSIS

- Absence of peroxisomes in hepatic cells (on biopsy).
- Genetic testing available.

EXTRAHEPATIC BILIARY ATRESIA

DEFINITION

Distal segmental bile duct obliteration with patent extrahepatic ducts up to porta hepatis.

EPIDEMIOLOGY

- Most common form (85%): Obliteration of entire extrahepatic biliary tree at/above porta.
- Occurs in 1 in 10,000 to 1 in 15,000 live births.

SIGNS AND SYMPTOMS

- Acholic stools (stools are very light in color, almost beige).
- ↑ incidence of polysplenia syndrome with heterotaxia, malrotation, levo-cardia, and intra-abdominal vascular anomalies.

DIAGNOSIS

- Ultrasound.
- Hepatobiliary scintigraphy.
- Liver biopsy.

TREATMENT

- Exploratory laparotomy and direct cholangiography to determine presence and site of obstruction.
- Direct drainage if lesion is correctable.
- Surgery if lesion is not correctable (liver transplant, Kasai procedure).

Hepatitis

- Continues to be major problem worldwide.
- Six known viruses cause hepatitis as their primary manifestation—A (HAV), B (HBV), C (HCV), D (HDV), E (HEV), and G (HGV).
- Many others cause hepatitis as part of their clinical spectrum—herpes simplex virus (HSV), cytomegalovirus (CMV), Epstein-Barr virus (EBV), rubella, enteroviruses, parvovirus.
- HBV is a DNA virus, whereas HAV, HCV, HDV, HEV, and HGV are RNA viruses.
- HAV and HEV are not known to cause chronic illness, but HBV, HCV, and HDV cause important morbidity and mortality through chronic infection.
- HAV causes most cases of hepatitis in children.
- HBV causes one-third of all cases; HCV found in 20%.

HEPATITIS A

DEFINITION

- RNA-containing member of the Picornavirus family.
- Found mostly in developing countries.
- Causes acute hepatitis only.
- Two-thirds of children are asymptomatic.
- Transmission by person-to-person contact; spread by fecal-oral route.
- Percutaneous transmission rare, maternal-neonatal not recognized.
- ↑ risk in child care centers, contaminated food or water, or travel to endemic areas.
- Mean incubation 4 weeks (15–50 days).

SIGNS AND SYMPTOMS

- Abrupt onset with fever, malaise, nausea, emesis, anorexia, and abdominal discomfort.
- Diarrhea common.
- Almost all recover but may have relapsing course over several months.
- Jaundice.

DIAGNOSIS

- Consider when history of jaundice in family contacts or child care playmates or travel history to endemic region.
- Serologic criteria:
    - Immunoglobulin M (IgM) anti-HAV presents at onset of illness and disappears within 4 months. May persist for >6 months (acute infection). IgG is detectable at this point.
    - ↑ alanine transaminase (ALT), aspartate transaminase (AST), bilirubin, and gamma-glutamyl transpeptidase (GGT).

TREATMENT

- Careful hand washing.
- Vaccines available (preferred over immunoglobulin in children >2 years).

HEPATITIS B

DEFINITION

- DNA virus from the Hepadnaviridae family.
- Most important risk factor for infants is perinatal exposure to hepatitis B surface antigen (HbsAg)-positive mother.

SIGNS AND SYMPTOMS

- Many cases asymptomatic.
- ↑ ALT prior to lethargy, anorexia, and malaise (6–7 weeks post exposure).
- May be preceded by arthralgias or skin lesions and rashes.
- May see extrahepatic conditions, polyarteritis, glomerulonephritis, aplastic anemia.
- Jaundice: Icteric skin and mucous membranes.
- Hepatosplenomegaly and lymphadenopathy common.

DIAGNOSIS

- Routine screening requires assay of two serologic markers: HbsAg (all infected persons, ↑ when symptomatic) and hepatitis B core antigen (HbcAg) (present during acute phase, highly infectious state).

> **EXAM TIP**
>
> Chronic hepatitis B is a risk factor for hepatocellular carcinoma.

- HbsAg falls prior to symptom resolution; IgMAb to HbcAg also required because it is ↑ early after infectivity and persists for several months before being replaced by immunoglobulin G (IgG) anti-HbcAg.
- HbcAg most valuable; it is present as early as HbsAg and continues to be present later when HBsAg disappears.
- Only anti-HbsAg detected in persons immunized with hepatitis B vaccine, whereas anti-HbsAb and anti-HbcAg are seen in persons with resolved infection.

PREVENTION

- Screening blood donors.
- Screening pregnant women to prevent vertical transmission.

TREATMENT

- No available medical treatment effective in majority of cases.
- Interferon-α is approved treatment in children.
- Liver transplant for patients with end-stage HBV.

HEPATITIS C

DEFINITION

- Single-stranded RNA virus.
- Perinatal transmission described but uncommon except with high-titer HCV.

SIGNS AND SYMPTOMS

- Acute infection similar to other hepatitis viruses.
- Mild and insidious onset.
- Fulminant liver failure rare.
- After 20–30 years, 25% progress to cirrhosis, liver failure, or primary hepatocellular carcinoma.
- May see cryoglobulinemia, vasculitides, and peripheral neuropathy (extrahepatic).

DIAGNOSIS

- Detection of antibodies to HCV or direct testing for RNA virus.
- Polymerase chain reaction (PCR) detection possible.
- ↑ ALT.
- Confirmed by liver biopsy.

TREATMENT

- Treat to prevent progression to future complications.
- INF-α_{2b} for patients with compensated liver disease (response rate long term ~25%).
- May use with ribavirin for higher frequency of sustained response.

HEPATITIS D (DELTA AGENT)

DEFINITION

- Smallest known animal virus.
- Cannot produce infection without HBV infection (coinfective or super-infection).
- Transmission by intimate contact.

SIGNS AND SYMPTOMS

- Similar to but more severe than other hepatitis viruses.
- In coinfection, acute hepatitis is more severe, risk of developing chronic hepatitis low; in superinfection, risk of fulminant hepatitis is highest.

DIAGNOSIS

Detect IgM antibody to HDV (2–4 weeks after coinfection, 1 week after superinfection).

PREVENTION

No vaccine for hepatitis D, but can minimize against hepatitis B (needs hepatitis B to infect).

HEPATITIS E

DEFINITION

- RNA virus with nonenveloped sphere shape with spikes (similar to caliciviruses).
- Non-A, non-B hepatitis.

SIGNS AND SYMPTOMS

- Similar to HAV, but more severe.
- No chronic illness.
- High prevalence of fulminant hepatic failure and death in pregnant women.

DIAGNOSIS

- Antibody to HEV exists.
- IgM and IgG assays available.
- Can detect viral RNA in stool and serum by PCR.

PREVENTION

No vaccines available.

HEPATITIS G

DEFINITION

- Single-stranded RNA virus of Flaviviridae family.
- Virus not yet isolated.
- Reported in all population groups in ~1.5% U.S. blood donors.
- One percent transmission through transfusions but also by organ transplant.
- Vertical transmission occurs.

SIGNS AND SYMPTOMS

- Symptoms associated with hepatic inflammation.
- Coinfection does not worsen course of HBV or HCV.

DIAGNOSIS

Only PCR assays available for testing.

TREATMENT

No method available.

NEONATAL HEPATITIS

DEFINITION

- Hepatic inflammation of unknown etiology.
- Most result from systemic disease (e.g., sepsis).
- Also caused by CMV, HSV, human immunodeficiency virus (HIV).
- Nonviral causes include congenital syphilis and toxoplasmosis.
- HBV results in asymptomatic infection.

SIGNS AND SYMPTOMS

- Jaundice.
- Vomiting.
- Poor feeding.
- ↑ liver enzyme levels.
- Fulminant hepatitis.

TREATMENT

- Antibiotics for bacteria-associated hepatitis.
- Acyclovir for HSV.
- Ganciclovir and foscarnet for CMV.

AUTOIMMUNE (CHRONIC) HEPATITIS

DEFINITION

- Hepatic inflammatory process manifested by ↑ serum aminotransferase and liver-associated autoantibodies.
- Variable severity.
- Fifteen to twenty percent of cases associated with HBV.
- Clinical constellation that suggests immune-mediated disease process responsive to immunosuppressive treatment.

SIGNS AND SYMPTOMS

- Variable.
- May mimic acute viral hepatitis.
- Onset insidious.
- May be asymptomatic or may have fatigue, malaise, anorexia, or amenorrhea.
- Extrahepatic signs include arthritis, vasculitis, and nephritis.
- Mild to moderate jaundice.

DIAGNOSIS

- Detection of autoantibodies (anti-smooth muscle, anti-liver-kidney-microsome, anti-soluble live antigen).
- Liver biopsy.
- Exclude other disease.

TREATMENT

- Corticosteroid.
- Azathioprine.

Reye Syndrome

DEFINITION

- Acute encephalopathy and fatty degeneration.
- Hepatic dysfunction (>3-fold ↑ in ALT, AST, and/or ammonia levels).

- No other explanation for cerebral edema or hepatic abnormality.
- ↓ incidence secondary to awareness about association with the use of aspirin during the illness relation to acetylsalicylic acid (ASA) ingestion, most commonly associated with influenza and varicella.
- Many other "Reye-like" syndromes exist (medium-chain fatty-acid oxidation defect or urea-cycle defects).

SIGNS AND SYMPTOMS

- Stereotypic, biphasic course.
- Usually see prodromal illness, upper respiratory infection (URI), influenza, or varicella chickenpox initially, followed by a period of apparent recovery, then see abrupt onset of protracted vomiting 5–7 days after illness onset.
- May see delirium, combative behavior, and stupor.
- First neurologic manifestation: Lethargy.
- Neurologic symptoms including seizures, coma, or death.
- Slight to moderate liver enlargement.

DIAGNOSIS

- Based on clinical staging.
- Liver biopsy may show yellow to white color because of high triglyceride content.

TREATMENT

- Airway, breathing, circulation (ABC) is the priority.
- Bedside glucose (provide dextrose to manage hypoglycemia).
- No specific treatment.
- Control intracranial pressure (ICP) secondary to cerebral edema.
- Supportive management depending on clinical stage.

α_1-Antitrypsin Deficiency

DEFINITION

- α_1-Antitrypsin is a major protease inhibitor (PI).
- A small percentage of homozygous patients have neonatal cholestasis, and later in childhood cirrhosis.
- Present in >20 codominant alleles; only a few associated with defective PI.
- PI ZZ usually predisposes to clinical deficiency (<20% develop neonatal cholestasis).

SIGNS AND SYMPTOMS

- Variable course.
- Jaundice, acholic stools, and hepatomegaly in first week of life; jaundice clears by second to fourth month.
- May have complete resolution, persistent liver disease, or cirrhosis.
- Older children may present with chronic liver disease.

DIAGNOSIS

- Determination of α_1-antitrypsin phenotype.
- Confirmed by liver biopsy.

TREATMENT

- Liver transplant curative.
- No other effective treatment.

EXAM TIP

The most likely clinical manifestation of α_1-antitrypsin deficiency in the newborn is jaundice (neonatal cholestasis).

Wilson Disease

DEFINITION

- Autosomal-recessive disease characterized by excessive copper deposition in brain and liver.
- Worldwide incidence: 1/30,000.

SIGNS AND SYMPTOMS

- Variable manifestations, including:
    - Asymptomatic in early stages.
    - Jaundice, abdominal pain.
    - Hepatomegaly, subacute/chronic hepatitis or fulminant liver failure.
    - Portal hypertension, ascites, edema, esophageal bleeding.
    - Delayed puberty, amenorrhea, or coagulation defect.
    - Psychosis.
    - Tremors.
- Kayser-Fleischer rings are greenish-brown rings of pigment seen at the limbus of the cornea, reflecting deposits of copper in Descemet membrane. They can be seen with the naked eye in patients with blue eyes. In patients with dark eyes, a slit lamp is often needed to identify them. Ninety percent of patients with Wilson disease have Kayser-Fleischer rings.

DIAGNOSIS

Copper indices reveal:
- Low serum ceruloplasmin.
- High serum copper level.
- Liver biopsy for histochemistry and copper quantification.
- Genetic testing, including siblings.

TREATMENT

- Disease is always fatal if left untreated.
- Zinc: Newest Food and Drug Administration (FDA)-approved agent; works by blocking absorption of copper in GI tract.
- Copper-chelating agents to ↓ deposition (e.g., penicillamine and trientine).
- Restrict copper intake. Foods high in copper include (Source: *Mayo Clinic Diet Manual*):
    - Lamb, pork, pheasant, quail, duck, goose, squid, salmon, all organ meats (liver, heart, kidney, brain), all shellfish (oysters, scallops, shrimp, lobster, clams, crab), meat gelatin, soy protein, meat substitutes, tofu, all nuts and seeds, dried beans (soybeans, lima beans, baked beans, garbanzo beans, pinto beans), dried peas, and lentils.
    - Soy milk, chocolate milk, cocoa, chocolate.
    - Nectarines, commercially dried fruits (okay if dried at home).
    - Mushrooms, sweet potatoes, vegetable juice cocktail.
    - Barley, bran breads and bran cereals, cereals with >0.2 mg of copper per serving (check label), millet, soy flour, soy grits, wheat germ, brewer's yeast.
- Patients with hepatic failure require liver transplant.

Hepatic Neoplasms

HEPATOBLASTOMA

DEFINITION

- Rare in children.
- Fewer than 65% of malignant tumors are hepatoblastomas.
- Associated with Beckwith-Wiedemann syndrome.
- Usually arises from the right lobe of the liver and is unifocal.
- Two histologic types—epithelial and mixed.

SIGNS AND SYMPTOMS

- Generally present in first 18 months of life.
- Large, asymptomatic abdominal mass.
- Abdominal distention and ↑ liver size.
- Weight loss, anorexia, vomiting, and abdominal pain (as disease progresses).
- May spread to regional lymph nodes.

DIAGNOSIS

- α-Fetoprotein (AFP) level helpful as marker.
- Diagnostic imaging includes ultrasound to detect mass, CT, or magnetic resonance imaging (MRI).

TREATMENT

- Complete resection of tumor.
- Cisplatin and doxorubicin adjuvant chemotherapy.
- More than 90% survival with multimodal treatment (surgery with chemotherapy).

Liver Abscesses

ECHINOCOCCUS

DEFINITION

- Most widespread cestode.
- Transmitted from domestic and wild canine animals.
- Two species: *Echinococcus granulosus* and the more malignant *Echinococcus multilocularis.*
- Hosts are dogs, wolves, coyotes, and foxes that eat infected viscera.
- Humans are infected by ingesting contaminated food or water.

SIGNS AND SYMPTOMS

- Majority of cysts in liver; most never symptomatic.
- Early, nonspecific symptoms; later on, ↑ abdominal girth, hepatomegaly, vomiting, or abdominal pain.
- Anaphylaxis secondary to rupture and spillage of contents.
- Second most common site is lungs; symptoms include chest pain and coughing or hemoptysis.

DIAGNOSIS

- Clinical.
- Ultrasound.
- Serologic studies have high false-negative rate.

TREATMENT

- Surgery.
- May be CT guided.
- If not amenable to surgery, may be treated with albendazole.

AMEBIC ABSCESS

DEFINITION

A very serious manifestation of disseminated infection.

SIGNS AND SYMPTOMS

Abdominal pain, distention, and liver enlargement with tenderness.

DIAGNOSIS

- May see slight leukocytosis.
- Moderate anemia.
- ↑ ESR.
- Nonspecific ALT ↑.
- Stool exam negative in >50% of patients.
- CT or MRI.

TREATMENT

- Metronidazole.
- Chloroquine.
- Aspiration of left-lobe abscesses if rupture is imminent.

Respiratory Disease

Respiratory Disease in Children

- Pediatric respiratory disorders are responsible for a number of acute and chronic health conditions and are a leading cause of pediatric emergency room visits and hospitalizations.
- Anatomic and physiologic differences in the young child versus adults predispose the pediatric patient to more severe presentations.

Respiratory Distress

- Tachypnea (See Table 12-1 for normal respiratory rates by age).
- Intercostal retractions.
- Nasal flaring (indicates ↑ effort is needed to breathe).
- Use of accessory muscles for breathing (e.g., abdominals, sternocleidomastoids).
- Restlessness, agitation.
- Somnolence or lethargy may be due to severe hypoxia or hypercarbia.
- Pallor, cyanosis.
- Wheezing may or may not be present.
- **Stridor** is an inspiratory sound that localizes respiratory distress to the upper airway.
- **Grunting:**
  - Due to exhalation against a partially closed glottis.
  - Occurs during expiration.
  - Indicates moderate to severe hypoxia.

Upper Respiratory Infection (the Common Cold)

A 7-year-old girl is well when she leaves for school, but arrives home afterwards with a sore throat and runny nose. She is also complaining of cough, sneezing, and facial heaviness. *Think: Rhinovirus.* Rhinovirus colds frequently start as a sore or "scratchy" throat with runny nose.

A 17-year-old adolescent has acute onset of fever, cough, conjunctivitis, and pharyngitis. *Think: Adenovirus.* Characteristic presentation: Pharyngitis, rhinitis, and conjunctivitis.

EXAM TIP

Infants and young children have smaller diameter airways, proportionally larger tongues, a floppy epiglottis, a higher and more anterior larynx leading to more acute respiratory illnesses.

WARD TIP

Respiratory arrest is the most common cause of cardiac arrest in children.

EXAM TIP

- **Stertor** low-pitched, sounds like nasal congestion experienced with a cold, or like the sound made with snoring.
- **Stridor** is a higher-pitched noise that occurs with obstruction in or just below the voice box.
- **Wheezing** is a high-pitched noise that occurs during expiration due to narrowing, spasm, or obstruction of the smaller airways in the lungs.

EXAM TIP

- Inspiratory stridor suggests a laryngeal obstruction.
- Expiratory stridor implies tracheobronchial obstruction.
- Biphasic stridor suggests a subglottic or glottic anomaly.

WARD TIP

Rhinovirus is an RNA virus while adenovirus is a DNA virus.

T A B L E   1 2 - 1 .   **Normal Respiratory Rates in Children**

AGE	Birth–6 Weeks	6 Weeks–2 Years	2–6 Years	6–10 Years	Over 10 Years
RESPIRATORY RATE	45–60/min	22–37/min	20–30/min	18–25/min	12–20/min

DEFINITION

Multi-etiology illness with a constellation of symptoms including cough, congestion, and rhinorrhea. Upper respiratory infections (URIs) are the most common pediatric ED presentation.

ETIOLOGY

- **>200 viruses**—especially rhinoviruses (one-third), parainfluenza, respiratory syncytial virus (RSV), adenovirus, influenza, metapneumovirus.
- Risk factors: Child care facilities, smoking, passive exposure to smoke, low income, crowding, and psychological stress.

EPIDEMIOLOGY

- Most frequent illness of childhood (three to eight episodes per year).
- Most common medical reason to miss school.
- Occurs in fall and winter especially.

SIGNS AND SYMPTOMS

- Nasal and throat irritation.
- Sneezing, nasal congestion, rhinorrhea.
- Sore throat, postnasal drip.
- Low-grade fever, headache, malaise, and myalgia.
- Possible complications include otitis media, sinusitis, and trigger asthma.
- Infants have a variable presentation—feeding and sleeping are difficult due to congestion, vomiting may occur after coughing, may have diarrhea.

TREATMENT

- Supportive including oral hydration, humidified air, topical saline drops to nares.
- Avoid aspirin and over-the-counter cough suppressants or decongestants.
- Direct therapy toward specific symptoms.

Influenza

DEFINITION

Viral respiratory illness.

ETIOLOGY

- Influenza A and B—with varying epidemics associated with certain subtypes (H1N1).
- Influenza C—sporadic.

EPIDEMIOLOGY

Common over the winter months.

SIGNS AND SYMPTOMS

- Incubation period: 1–3 days.
- Sudden onset of fever, frequently with chills, headache, malaise, diffuse myalgia, and nonproductive cough.
- Conjunctivitis, pharyngitis.
- Typical duration of febrile illness is 2–4 days.
- Complications include otitis media, pneumonia, myositis, and myocarditis.
- Diarrhea and vomiting.

WARD TIP

Mucopurulent rhinitis may accompany a common cold and doesn't necessarily indicate sinusitis; it is not an indication for antibiotics.

WARD TIP

The best treatment for the common cold is to ↑ oral fluids, *not* pharmacologic treatment.

EXAM TIP

Infants are *obligate* nasal breathers; the common cold can trigger respiratory distress in the young infant due to mucous obstruction of the nares. Nasal saline drops and suctioning is important to relieve the obstruction.

WARD TIP

Aspirin is avoided in young children due to theoretical risk of Reye syndrome.

EXAM TIP

Influenza is an orthomyxovirus.

WARD TIP

Diagnosis of influenza depends on epidemiologic and clinical considerations.

WARD TIP

Increased risk for bacterial superinfection; most common organisms are *Staphylococcus aureus* and *Streptococcus pneumoniae*.

DIAGNOSIS

- Nasal swab or nasal washing.
- During epidemic, clinical signs can be used to save on test costs.

TREATMENT

- Symptomatic treatment is appropriate for healthy children—fluids, rest, acetaminophen, or ibuprofen.
- For children at risk, see Table 12-2 for drug options.
- Pregnant patients with H1N1 should receive a 5-day course of antiviral treatment.
- Oseltamivir is preferred during pregnancy.

VACCINE

Intramuscular
- Now recommended for all children over age 6 months, with priority given to high-risk groups.
- High-risk groups include children with chronic diseases such as asthma, renal disease, diabetes, and any other form of immunosuppression.
- Best administered mid-September to mid-November since the peak of the flu season is late December to early March.
- Antibodies take up to 6 weeks to develop in children. Consider prophylaxis in high-risk children during this period.
- Since composition of influenza virus changes, the flu vaccine needs to be administered every year.
- Vaccine is a killed virus and therefore cannot cause the flu.
- Not approved for children <6 months of age.

Intranasal
- Live, attenuated vaccine available for children >5 years old.
- No longer recommended as of 2016–2017 season due to concerns regarding its effectiveness.

TABLE 12-2. Drug Treatments for Influenza (All Pregnancy Category C)

	INDICATIONS	AGE GROUPS	RX DOSE	ADVERSE EFFECTS
Amantadine	For type A only Both prophylaxis and treatment	Age >1 year	200 mg PO bid × 7 days	Central nervous system and gastrointestinal effects
Rimantadine	For type A only	Px: Age >12 years	100 mg PO bid × 7 days	Same as for amantadine, but less frequent and less severe
Peramivir	For Type A and B Treatment only	Tx: Age >18 years	600 mg IV × 1 dose	Diarrhea
Zanamivir	For types A and B Treatment and prophylaxis	Tx: >7years Px: >5 years	Tx: Two inhalations (10 mg) bid × 5 days Px: Two inhalations (10 mg) once daily × 5 days	Wheezing in patients with asthma, sinusitis, nausea, diarrhea
Oseltamivir	For types A and B Treatment and prophylaxis	Tx: >2weeks Px: >3 months	Weight-based dosing × 5 days	Nausea, vomiting, diarrhea, abdominal pain, bronchitis, dizziness, headache

Tx, treatment; Px, prophylaxis.

Parainfluenza

ETIOLOGY

- Type 1 and 2—seasonal, less common.
- Type 3—endemic, more prevalent.
- See Table 12-3.

PATHOGENESIS

- Infects epithelial cells of the nose and oropharynx first.
- Moves distally to ciliated/alveolar cells of large and small airway epithelium.

SIGNS AND SYMPTOMS

- Incubation period: 2–6 days.
- Causes:
  - Colds.
  - Pharyngitis.
  - Otitis media.
  - Croup.
  - Bronchiolitis.
- Can be severe in immunocompromised patients.

TREATMENT

Specific antiviral therapy is not available.

Croup

CROUP (ACUTE LARYNGOTRACHEOBRONCHITIS)

An 18-month-old boy awakes from his sleep at night with sudden onset of inspiratory stridor and a barking cough with difficulty breathing that calms down on route to the emergency department. He has had a runny nose and cough for 2 days. On examination, he has a barky cough, and inspiratory stridor only with agitation. *Think: Croup.*

EXAM TIP

Parainfluenza is a paramyxovirus.

WARD TIP

Parainfluenza types 1 and 2 cause croup; type 3 causes bronchiolitis and pneumonia; type 4 is a cause of the common cold.

WARD TIP

Croup is the most common cause of stridor in a febrile child.

TABLE 12-3.   **Respiratory Infections and Pathogens**

RESPIRATORY INFECTION	MOST COMMON PATHOGEN	PARTICULAR SIGNS AND SYMPTOMS
Croup	Parainfluenza virus	Barking cough, steeple sign
Epiglottitis	*H. influenzae* type B	Tripod position, thumb sign
Tracheitis	*S. aureus, H. influenzae* type B	Rapidly progressive
Bronchiolitis	Respiratory syncytial virus	Paroxysmal wheezing
Bronchitis	Viral	Productive cough
Pharyngitis	Viral, group A strep	Sore throat, tonsillar involvement
Bacterial pneumonia	*S. pneumoniae*	Productive cough, lobar consolidation
Pulmonary abscess	*S. aureus*	Cavity with air-fluid level

FIGURE 12-1. Radiograph demonstrating steeple sign of croup. Note narrowing of airway (arrow). (Used with permission from Dr. Gregory J. Schears.)

DEFINITION

- Viral infection of upper respiratory tract with inflammation and narrowing in the subglottic airway.
- A subset of patient swill have non-infectious spasmodic croup which only occurs at night and is of sudden onset with very mild or no antecedent URI symptoms.

ETIOLOGY

Parainfluenza virus types 1 and 2.

EPIDEMIOLOGY

Occurs in children 3 months to 3 years of age in fall and winter months with increased risk in males.

SIGNS AND SYMPTOMS

- Inspiratory stridor.
- Seal-like, barking cough with retractions and nasal flaring.
- May have coryza, fever, and congestion.
- Can progress to agitation, hypoxemia, hypercapnia, tachypnea, and tachycardia.
- Most cases are mild and last 3–7 days.
- Symptoms worse at night, with sudden onset of symptoms.

DIAGNOSIS

- Diagnosis is made clinically.
- X-ray usually not necessary. Consider only if diagnosis is in doubt.
- Steeple sign—narrowing of tracheal air column just below the vocal cords (see Figure 12-1).
- Ballooning—distention of hypopharynx during inspiration.
- Differentiate croup from epiglottitis.
- Severity can be measured by the Westley Croup Score (see Table 12-4).
  - 0–2: mild croup.
  - 3–7: moderate croup.
  - 8–11: severe croup.
  - 12–17: impending respiratory failure.

TREATMENT

- Position of comfort. Cool mist humidification has limited role based on evidence.
- Mild—dexamethasone (PO, IV, IM), may discharge if no stridor at rest.
- Moderate—dexamethasone, racemic epinephrine neb (0.25 mL in 3–5 mL of normal saline [NS]), observe 3–4 hours, if improved may discharge, if symptoms persist or worsen, repeat racemic epinephrine neb, and admit.
- Severe—racemic epinephrine, early use of corticosteroids, admit to intensive care unit (ICU), consider heliox.
- Dexamethasone 0.6 mg/kg (lower dose [0.15 mg/kg] has also shown to be effective) is advantageous due to longer half-life that corresponds with length of typical illness.
- Admission criteria:
  - Persistent stridor (especially at rest).
  - Respiratory distress.
  - Multiple doses of racemic epinephrine.
  - Possibility of alternate diagnosis.

T A B L E   1 2 - 4 .   Westley Croup Score: Classification of Croup Severity

	NUMBER OF POINTS ASSIGNED FOR THIS FEATURE					
FEATURE	0	1	2	3	4	5
Chest wall retractions	None	Mild	Moderate	Severe		
Stridor	None	With agitation	At rest			
Cyanosis	None				With agitation	At rest
Level of consciousness	Normal					Disoriented
Air entry	Normal	Decreased	Markedly decreased			

(Adapted with permission from National Asthma Education & Prevention Program Expert Panel Report 3: Guidelines for the Diagnosis & Management of Asthma NHLBI guidelines, Summary Report 2007: 54)

CORTICOSTEROIDS IN RESPIRATORY PROBLEMS

- Dexamethasone (IM, IV, or PO 0.6 mg/kg).
- Side effects associated with short-term steroid use are minimal.

Epiglottitis

> A 4-year-old unvaccinated boy brought to the ED is flushed, making high-pitched noises on forced inspiration, leaning forward in his mother's lap, and drooling. His illness started with fever and sore throat and rapidly progressed to difficulty swallowing, drooling, restlessness, and stridor or air hunger. He appeared toxic and anxious. Lateral neck x-ray shows thumb sign. *Think: Epiglottitis,* and get him to an operating room (OR) to intubate and treat!
> The classic presentation: "three Ds" (drooling, dysphagia, and distress).

See Figure 12-2.

DEFINITION

Acute, life-threatening infection of epiglottic and supraglottic tissues due to direct invasion of the epithelial layer by the organism.

ETIOLOGY

- *Haemophilus influenzae* type B.
- Other possible pathogens—*Streptococcus pyogenes, Streptococcus pneumoniae, Staphylococcus aureus.*

PATHOPHYSIOLOGY

Acute inflammation and edema of epiglottis, aryepiglottic folds, and arytenoids.

EPIDEMIOLOGY

- ↓ incidence due to *H. influenzae* type B vaccine (HiB).
- Usually 6–12 years of age, but can occur at any age.
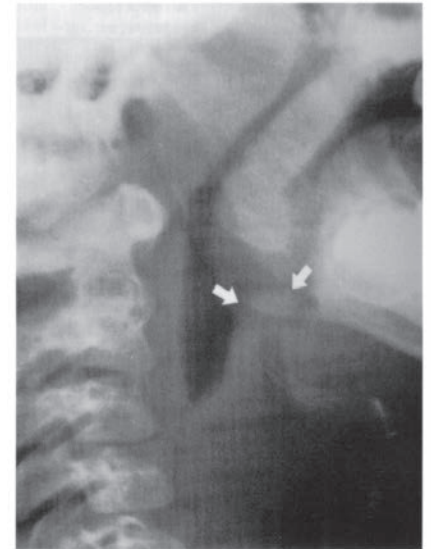
F I G U R E   1 2 - 2 .   Radiograph of lateral soft tissue of neck demonstrating epiglottitis. Note the thickening of the epiglottic and aryepiglottic folds (arrows). (Reproduced, with permission, from Schwartz DT, Reisdorff BJ. *Emergency Radiology.* New York: McGraw-Hill, 2000: 608.)

WARD TIP

Minutes count in acute epiglottitis.

WARD TIP

Primary source of pathogens in epiglottitis is from the posterior nasopharynx.

- Suspect in unvaccinated children and immunodeficient children.
- *H. influenzae* immunization has practically eliminated epiglottitis in young children.

SIGNS AND SYMPTOMS

- Sudden onset of inspiratory stridor and respiratory distress.
- Three Ds: Dysphagia, drooling, and distress.
- Tripod position—hyperextended neck, leaning forward, mouth open.
- Muffled voice ("hot potato" voice).
- High fever (usually the first symptom).
- Tachycardia is a constant feature.
- Cough is typically absent.
- Toxic appearing.
- Severe respiratory distress develops within minutes to hours.
- May progress to restlessness, pallor/cyanosis, coma, death.

DIAGNOSIS

- Laryngoscopy—swollen, cherry-red epiglottis.
- Lateral neck x-ray to confirm (portable x-ray should be obtained).
- Swollen epiglottis (thumbprint sign).
- Thickened aryepiglottic fold.
- Obliteration of vallecula.

TREATMENT

- **True medical emergency**—potentially lethal airway obstruction.
- Comfort.
- Anticipate.
- Secure airway (endotracheal intubation in OR).
- Ceftriaxone (100 mg/kg/day) 7–10 days.
- Rifampin prophylaxis for close contacts.

Bacterial Tracheitis

DEFINITION

- Rapidly progressive upper airway obstruction due to an invasive exudative bacterial infection of the soft tissues of the trachea.
- The larynx of healthy individuals is often colonized normally with bacteria, some of which are potential pathogens. These pathogens can extend, at least transiently, into the trachea.

ETIOLOGY

- *S. aureus* and *H. influenzae* type b.
- Also *Moraxella catarrhalis*.
- High association with preceding viral infections, especially influenza A infection.

SIGNS AND SYMPTOMS

- Often present with croup symptoms. Differentiation can be made by the presence of:
  - High fever.
  - Toxicity.
  - Inspiratory stridor (constant).
  - Purulent sputum.
- Tracheitis has features of both croup (stridor and croupy cough) and epiglottitis (high fever and toxic appearance).

DIAGNOSIS

- X-ray—may be normal or identical to croup. Look for **pseudomembrane** on lateral view.
    - Epiglottis size normal.
    - Tracheal narrowing.
    - Pseudomembrane.
- Bronchoscopy showing inflamed and exudate covered trachea.
- Copious purulent secretion distal to glottis.
- Secretions should be obtained for Gram stain and culture.

TREATMENT

- Secure an adequate airway (endotracheal intubation):
    - Should be performed in an operating room under anesthesia.
    - Suction endotracheal tube of purulent material to reduce obstruction.
- Specialty consultation: Ear, nose, and throat (ENT), and anesthesia.
- Ceftriaxone 100 mg/kg/day.
- Ampicillin-sulbactam 200 mg/kg/day.
- ICU admission even if intubation is not needed in order to monitor progression of disease.

Bronchiolitis

> A previously healthy 4-month-old who had rhinorrhea, cough, and a low-grade fever develops tachypnea, mild hypoxemia, and hyperinflation of lungs. *Think: RSV bronchiolitis.*
>
> Classic presentation: Acute onset of cough, wheezing, and ↑ respiratory effort after an upper respiratory tract prodrome (fever and runny nose), during the winter season.

DEFINITION

Viral infection of the lower respiratory tract (medium and small airways) which occurs after upper respiratory symptoms.

ETIOLOGY

- RSV—most common cause.
- Rhinovirus.
- Adenovirus.
- Parainfluenza 3.
- Influenza.
- Human metapneumovirus (hMPV): First recognized in 2001 and now increasingly implicated.
- Two or more viruses are found in one-third of children hospitalized with bronchiolitis.

PATHOPHYSIOLOGY

- Inflammatory obstruction (edema and mucus) of the bronchioles secondary to viral infection.
- Alterations in gas exchange are most frequently the result of mismatching of pulmonary ventilation and perfusion.
- Can lead to atelectasis.

EPIDEMIOLOGY

- Occurs in first 2 years of life.
- Reinfection is common.

EXAM TIP

X-rays are not definitive, nor essential for the diagnosis of bacterial tracheitis. The only definitive way to diagnose is by direct visualization by bronchoscopy.

WARD TIP

Bronchiolitis is the most common serious respiratory infection in children <2 years.

WARD TIP

The virus infects terminal bronchiolar epithelial cells.

EXAM TIP

RSV in fall and late winter; rhinovirus in spring and early fall typically.

EXAM TIP

RSV causes more than 50% of cases of bronchiolitis.

- Occurs in winter and early spring.
- Risks: Crowded conditions, not breast-fed, mothers who smoke, male gender.
- High-risk infants:
  - Cardiac disease.
  - Pulmonary disease and bronchopulmonary dysplasia.
  - Neuromuscular disease.
  - Premature infants.
  - Immunocompromised.

SIGNS AND SYMPTOMS

- Starts with mild upper respiratory symptoms: often profuse nasal discharge and congestion with or without fever.
- Respiratory distress gradually develops.
- Paroxysmal wheezing—common but may be absent, cough, dyspnea.
- Apneic spells—young infants should be monitored.
- Frequent complications include bacteremia, pericarditis, cellulitis, empyema, meningitis, and suppurative arthritis.
- Most common complication is hypoxia.
- Dehydration is the most common secondary complication.

DIAGNOSIS

- Mostly clinical but if other DDx are suspected, then consider additional testing.
- Viral detection in nasopharyngeal secretions via culture, polymerase chain reaction (PCR), or antigen detection.
- Chest x-ray (rule out pneumonia or foreign body)—hyperinflation of lungs, ↑ anteroposterior (AP) diameter of rib cage.
- Oxygen saturation is the single best objective predictor.

TREATMENT

- Low threshold for hospitalization for high-risk infants.
- Humidified oxygen.
- Nasal suctioning.
- Trial of nebulized albuterol although no long-term benefit shown (only 20–50% are responders, discontinue if no objective benefit).
- **Hypertonic saline neb tx**—potential to reduce airway edema and mucous plugging.
- Steroids not indicated in first episode of bronchiolitis.
- Respiratory isolation.
- Ribavirin (aerosol form) if high-risk patients such as immunocompromised, need for mechanical ventilation, or <6 weeks old.
- RSV intravenous immunoglobulin (RSV-IVIG) or palivizumab given prior to and during RSV season in high-risk infants <2 years old.

Bronchiectasis

A 7-year-old boy presents with an upper respiratory infection (URI) with productive cough (with purulent sputum). On examination, localized rales on the right side of his chest were noted. X-ray shows two discrete densities located in the right upper lobe of the lungs. *Think: Bronchiectasis.* Predisposition: Cystic fibrosis (CF) and ciliary dyskinesia.

DEFINITION

Abnormal and permanent dilatation of bronchi.

ETIOLOGY

- Viruses: Adenovirus, influenza virus.
- Bacteria: *S. aureus, Klebsiella*, anaerobes.
- Primary ciliary dyskinesia.
- Kartagener syndrome.
- Cystic fibrosis: *Pseudomonas aeruginosa*.
- α_1-antitrypsin deficiency.

PATHOPHYSIOLOGY

Consequence of inflammation and destruction of structural components of weak, easily collapsible bronchial walls and increased mucous plugs.

SIGNS AND SYMPTOMS

- Physical exam quite variable.
- Persistent or recurrent wet cough.
- Purulent sputum.
- Hemoptysis is not prevalent in children as it is in adults.
- Dyspnea.
- Crackles, rhonchi, less commonly wheezing.
- Clubbing.

DIAGNOSIS

- Chest x-ray.
- Bronchography.
- Computed tomographic (CT) scan (most sensitive imaging method).
- Sputum culture.

TREATMENT

- Elimination of underlying cause.
- Clearance of secretions in airway with chest physiotherapy.
- Mucolytic agents.
- Control of infection—antibiotics.
- Reversal of airflow obstruction—bronchodilators and anti-inflammatory meds.

> **EXAM TIP**
>
> TNF alpha, IL-1B, and IL-8 are increased in bronchiectasis, with or without CF.

> **WARD TIP**
>
> Rhonchi are coarse, expiratory breath sounds; crackles are inspiratory popping sounds.

> **WARD TIP**
>
> CXR shows dilated and thickened airways with linear atelectasis.

> **EXAM TIP**
>
> Cough is the most common symptom of chronic bronchitis.

Bronchitis

DEFINITION

Infection of conductive airways of lung.

ETIOLOGY

- Viruses: Influenza A and B, adenovirus, parainfluenza, rhinovirus, RSV, coxsackievirus.
- Bacteria: *Bordetella pertussis, M. pneumoniae, Chlamydia pneumoniae, S. pneumoniae*.

SIGNS AND SYMPTOMS

- Acute productive cough (<1 week).
- Rhinitis.
- Myalgia.

- Fever.
- No evidence of sinusitis, pneumonia, or chronic pulmonary disease.
- Normal arterial oxygenation.

TREATMENT

- Mostly self-limited.
- Bronchodilators may help.
- Antibiotics for high-risk patients.

Pharyngitis

DEFINITION

Infection of the tonsils and/or the pharynx.

ETIOLOGY

- Bacterial: Streptococcal pharyngitis
- Viruses: Rhinovirus, adenovirus, coxsackievirus, mononucleosis

SIGNS AND SYMPTOMS

- Viral pharyngitis:
    - Gradual onset.
    - Fever, malaise, throat pain.
    - Conjunctivitis, rhinitis, coryza, viral exanthem, diarrhea.
- Streptococcal pharyngitis (>2 years) (see Figure 12-3):
    - Headache, abdominal pain, and vomiting.
    - Fever (>104°F [40°C]).
    - Tonsillar enlargement with exudates.
    - Fetid odor.
    - Cervical adenopathy.
    - Palatal petechiae and uvular edema.
- It is not possible to distinguish clinically viral from bacterial pharyngitis, though high fever, cervical adenopathy, and absence of URI symptoms suggest bacterial etiology.

DIAGNOSIS

Rapid strep test: Rapid(DNase) antigen detection test (sensitivity 95–98%):
- Culture if negative.
- Treat if positive.

FIGURE 12-3.   **Streptococcal pharyngitis.** Note white exudates on top of erythematous swollen tonsils. (Reproduced, with permission, from Knoop KJ, Stack LB, Storrow AB, et al. *Atlas of Emergency Medicine*, 3rd ed. New York: McGraw-Hill, 2010: 115.)

TREATMENT

- Oral penicillin (25–50 mg/kg/day) for 10 days.
- Alternatively, intramuscular (IM) benzathine and procaine penicillin can be used (single dose, weight based).
- Macrolides or clindamycin for penicillin-allergic patients for 10 days.
- Tetracycline and sulfonamides should not be used to treat group A beta-hemolytic streptococci (GABHS) due to high resistance.
- Antibiotics are not indicated for pharyngitis negative for GABHS.

COMPLICATIONS

- Suppurative:
  - Peritonsillar abscess.
  - Retropharyngeal abscess.
  - Cervical adenitis.
  - Otitis media.
  - Sinusitis.
- Nonsuppurative:
  - Acute glomerulonephritis.
  - Acute rheumatic fever.

Pneumonia

> A 2-month-old with fever, tachypnea, and mottled skin has a chest x-ray showing infiltrate of the right upper lung lobe, a pneumatocele, and a pleural effusion. *Think:* S. aureus *pneumonia.*

> A previously healthy 9-year-old boy has a 7-day history of increasing cough, low-grade fever, and fatigue on exertion. Chest x-ray shows widespread diffuse perihilar infiltrates. *Think:* Mycoplasma *pneumonia.*
> Initially, nonproductive cough and no fever. Later, productive cough with fever, headache, coryza, otitis media, and malaise.

DEFINITION

Lower respiratory tract infection resulting in inflammation of lung parenchyma.

ETIOLOGY

- Viruses: RSV, influenza, parainfluenza, adenovirus.
- Bacteria: Less common, but more severe—*S. pneumoniae, S. pyogenes, S. aureus, H. influenzae* type B, *M. pneumoniae.*

SIGNS AND SYMPTOMS

- Respiratory distress including tachypnea, hypoxemia, increased work of breathing.
- Fever, productive cough, difficult feeding in infants.
- Afebrile pneumonia seen with *Chlamydia trachomatis* (pneumonitis syndrome) in infants.

DIAGNOSIS

- Lung exam, can hear crackles, decreased breath sounds, and dullness to percussion, egophany.

WARD TIP

Penicillin remains the drug of choice for GABHS.

WARD TIP

The more mucous membranes involved, the more likely an infection is viral.

WARD TIP

Round lobar pulmonary infiltrate on chest x-ray. *Think:* S. pneumoniae *pneumonia.*

WARD TIP

The most reliable sign of pneumonia is tachypnea.

WARD TIP

Consider pneumonia in children with neck stiffness (upper lobe) or acute abdominal (lower lobe) pain.

- Chest x-ray.
    - Viral (hyperinflation, perihilar infiltrate, hilar adenopathy, and atelectasis).
    - Bacterial (alveolar consolidation).
    - *Mycoplasma* (interstitial infiltrates).
    - Tuberculosis (hilar adenopathy).
    - *Pneumocystis* (reticulonodular infiltrates).
- CBC and blood culture (positive in 10–30% of bacterial cases).

TREATMENT

- **Inpatient:**
    - IV ampicillin is first line, second- or third-generation cephalosporin with or without vancomycin depending on degree of illness. Consider macrolide (pneumonitis syndrome) in 1- to 3–month-olds if suspected.
- **Outpatient:**
    - Patients should have normal O_2 saturation and be able to take oral fluids in order to be outpatients.
    - First line: High-dose amoxicillin. Alternative, second- or third-generation cephalosporin or azithromycin.

Pertussis

DEFINITION

- "Whooping cough."
- Highly infectious acute respiratory illness.

ETIOLOGY

- *Bordetella pertussis* gram-negative coccobacilli with exotoxin.
- Humans are the only known host.
- Whooping cough syndrome also may be caused by:
    - *Bordetella parapertussis.*
    - *M. pneumoniae.*
    - *C. trachomatis.*
    - *C. pneumoniae.*
    - Adenoviruses.

PATHOPHYSIOLOGY

- Pertussis toxin is a virulence protein that causes lymphocytosis and systemic manifestations.
- Aerosol droplet transmission.

EPIDEMIOLOGY

- Endemic, but epidemic every 3–4 years.
- 60 million cases/year worldwide.
- 500,000 deaths/year worldwide.
- July to October.
- Occurs in 1- to 5-year-olds worldwide, 50% <1-year-olds in the United States.

SIGNS AND SYMPTOMS

- Classic symptoms: Inspiratory whoop, paroxysmal cough, post-tussive emesis.
- Incubation period 1–2 weeks.
- Three stages: Catarrhal, paroxysmal, and convalescent.
- Duration: 6 weeks.

- Catarrhal stage: (1–2 weeks) Congestion, rhinorrhea, mild persistent cough.
- Paroxysmal stage (2–4 weeks):
  - Paroxysmal cough, with characteristic whoop following (chin forward, tongue out, watery, bulging eyes, purple face).
  - Fever is typically absent.
  - Post-tussive emesis and exhaustion.
- Convalescent stage: Number and severity of paroxysms plateaus.
- Each stage lasts ~2 weeks; shorter if immunized.
- Complications include apnea, physical sequelae of forceful coughing, brain hypoxia/hemorrhage, secondary infections (bacterial pneumonia is the cause of death).

DIAGNOSIS

- Diagnosis is primarily clinical:
  - Inspiratory whoop.
  - Post-tussive emesis.
  - Lymphocytosis.
- Chest x-ray—perihilar infiltrate or edema (butterfly pattern).
- Positive immunofluorescence test or PCR on nasopharyngeal secretions.

TREATMENT

- Goal—to ↓ spread of organism. Antibiotics do not affect illness in paroxysmal stage, which is toxin mediated.
- Macrolide antibiotic for patient and household contacts.
- Isolation until 5 days of therapy.
- Admit if:
  - Infant <3 months.
  - Apnea.
  - Cyanosis.
  - Respiratory distress.
  - DTP (diphtheria, tetanus, pertussis)/DTaP (diphtheria, tetanus, acellular pertussis) vaccine if not previously vaccinated.

Diphtheria

DEFINITION

Membranous nasopharyngitis or obstructive laryngotracheitis.

ETIOLOGY

- *Corynebacterium diphtheriae*, gram-positive bacillus.
- Humans are the only reservoir.

SIGNS AND SYMPTOMS

- Incubation period: 2–7 days.
- Erosive rhinitis with membrane formation and low-grade fever.
- Tonsillopharyngeal—sore throat, membranous exudate.
- Cardiac symptoms: Myocarditis, arrythmias.
- Tachycardia out of proportion to fever.

DIAGNOSIS

- Culture (nose, throat, mucosal, or cutaneous lesion).
- Material should be obtained from beneath the membrane or a portion of membrane.
- All *C. diphtheriae* isolates should be sent to diphtheria laboratory.

WARD TIP

Suspect pertussis if paroxysmal cough with skin color change.

WARD TIP

No single serologic test is diagnostic for pertussis.

WARD TIP

There is a risk of hypertrophic pyloric stenosis in infants younger than 6 weeks treated with oral macrolide antibiotics.

WARD TIP

DTaP vaccine series is given between 6 weeks and 7 years with booster TDaP given after age 11 years.

WARD TIP

For treatment of diphtheria, antibiotics are not a substitute for antitoxin.

WARD TIP

Most tuberculosis infections in children are asymptomatic with positive PPD.

TREATMENT

- Antitoxin (obtained from CDC)—dose depends on:
    - Site of membrane.
    - Degree of toxic effects.
    - Duration of illness.
- Antibiotics:
    - Erythromycin or penicillin G for 14 days.
    - Elimination of organism should be documented by two consecutive cultures.

Tuberculosis (TB)

DEFINITION

- Signs and symptoms and/or radiographic manifestations caused by *M. tuberculosis* are apparent.
- May be pulmonary, extrapulmonary, or both.

ETIOLOGY

Mycobacterium tuberculosis—acid fast bacilli.

PATHOPHYSIOLOGY

Primary portal of entry into children is lung.

EPIDEMIOLOGY

- Children are never the primary source (look for adult contacts).
- Risk factors:
    - Urban living.
    - Low income.
    - Recent immigrants.
    - HIV.

SIGNS AND SYMPTOMS

- Chronic cough (nonproductive) for more than 3 weeks.
- Hemoptysis.
- Fever.
- Night sweats.
- Weight loss or failure to thrive.
- Anorexia.
- Lymphadenopathy.
- Present to ED with:
    - Primary pneumonia.
    - Miliary TB (may mimic sepsis).

DIAGNOSIS

- When to suspect TB:
    - Hilar adenopathy.
    - Pulmonary calcification or caseating granulomas.
    - Pneumonia with infiltrate and adenopathy.
    - Pneumonia with pleural effusion.
    - Painless unilateral cervical adenopathy (scrofula).
    - Meningitis of insidious onset.
    - Bone or joint disease.
    - When any of the above are unresponsive to antibiotics.

WARD TIP

A patient may develop TB despite prior bacillus Calmette-Guérin (BCG) vaccination.

WARD TIP

A positive PPD skin test results from infection, not from exposure.

WARD TIP

Asymptomatic children with a positive PPD should be considered infected and get treatment.

WARD TIP

All cases of active TB should be referred to public health department.

WARD TIP

Persons with TB should be tested for HIV.

- PPD test (Mantoux test).
- QuantiFERON®-TB Gold test.
- Culture (gastric aspirates, sputum, pleural fluid, cerebrospinal fluid, urine, or other body fluids).
- Look for the adult source.
- Acid-fast stain or PCR.

TREATMENT

- Prompt treatment necessary as in very young, can disseminate quickly.
- Two to four or more drugs (isoniazid, rifampin, pyrazinamide, ethambutol, streptomycin) for a minimum of 6 months for active disease.
- Isoniazid for 9 months for latent disease.

Cystic Fibrosis (CF)

A 3-year-old child presents with constant cough with sputum. He has had six episodes of pneumonia, with *Pseudomonas* being isolated from sputum; loose stools; and is at the 20th percentile for growth. *Think: CF.*

CF is an inherited multisystem disorder resulting in chronic lung disease, exocrine pancreatic insufficiency, and failure to thrive.

DEFINITION

Disease of exocrine glands that causes viscous secretions:
- Chronic respiratory infection.
- Pancreatic insufficiency.
- ↑ electrolytes in sweat.

ETIOLOGY

- Defect of cyclic adenosine monophosphate (cAMP)–activated chloride channel of epithelial cells in pancreas, sweat glands, salivary glands, intestines, respiratory tract, and reproductive system.
- Autosomal recessive.

PATHOPHYSIOLOGY

- Decreased chloride secretion from cells in lungs and GI tract.
- ↑ osmotic pressure inside cells attracts water and → thick secretions.

EPIDEMIOLOGY

- Most common cause of severe, chronic lung disease in children.
- One in 2000–3000 live births (Caucasians).

SIGNS AND SYMPTOMS

- Respiratory:
  - **Cough (persistent and productive)**—most common pulmonary symptom.
  - Wheezing, dyspnea, exercise intolerance.
  - Bronchiectasis, recurrent pneumonia.
  - Sinusitis, *nasal polyps.*
  - Reactive airway disease, hemoptysis which results in anemia.
  - ↑ AP chest diameter.
  - Hyperresonant lungs.
  - Clubbing of nails.

WARD TIP

Most common extra-pulmonary manifestation of TB in children is involvement of superficial lymph nodes and CNS involvement.

WARD TIP

TB in children <4 years of age is much more likely to disseminate; prompt and vigorous treatment should be started when the diagnosis is suspected.

EXAM TIP

Cystic fibrosis is the most common lethal inherited disease of Caucasians.

EXAM TIP

The gene for cystic fibrosis is CFTR; the mutation is deletion of delta F508 on chromosome 7.

WARD TIP

A patient with severe CF breathing room air can have an arterial blood gas (ABG) showing ↓ chloride and ↑ bicarbonate.

- Gastrointestinal (GI):
    - **Failure to thrive.**
    - Meconium ileus (10%).
    - Constipation, rectal prolapse.
    - Intestinal obstruction.
    - Pancreatic insufficiency:
        - **Malabsorption with steatorrhea.**
        - Fat-soluble vitamin deficiencies.
        - Glucose intolerance.
    - Biliary cirrhosis (uncommon): Jaundice, ascites, hematemesis from esophageal varices.
- Reproductive tract: ↓/absent fertility—female, thick cervical secretions; male, azoospermic.
- Sweat glands:
    - Salty skin.
    - Hypochloremic alkalosis in severe cases.
- Complications may include pneumothorax, chronic pulmonary hypertension, cor pulmonale, atelectasis, allergic bronchopulmonary aspergillosis, respiratory failure, gastroesophageal reflux.

DIAGNOSIS

- Sweat test—chloride concentration >60 mEq/L (gold standard).
- Routine newborn screening done in all 50 states by IRT (immunoreactive trypsinogen) assay (↑) and DNA analysis (CFTR mutations). A sweat test is performed after 2 weeks old.
- Genetic studies.
- *In utero* screen available.
- Pulmonary function tests (PFTs): Obstructive and restrictive abnormalities.
- Prenatal diagnosis via gene proves CF mutations or linkage analysis.

TREATMENT

- Multidisciplinary team approach—pediatrician, physiotherapist, dietitian, nursing staff, teacher, child, and parents.
- Respiratory:
    - Chest physical therapy to promote mucociliary clearance.
    - Exercise.
    - Coughing to move secretions and mucous plugs.
    - Bronchodilators.
    - Normal saline aerosol.
    - Anti-inflammatory medications.
    - Dornase-alpha nebulizer (breaks down DNA in mucus).
- Pancreatic/digestive:
    - Enteric coated pancreatic enzyme supplements (add to all meals).
    - Fat-soluble vitamin supplements.
    - High-calorie, high-protein diet.
- Antibiotics—sputum cultures used to guide antibiotic choice. Pseudomonal infections are especially common. Macrolide antibiotics are most commonly used.
- Lung transplant.
- Gene therapy is being aggressively studied.

PROGNOSIS

Advances in therapy have ↑ life expectancy into adulthood.

Tonsils/Adenoids

TONSILLITIS/ADENOIDITIS

DEFINITION

Inflammation of:
- Tonsils—two faucial/palatine tonsils.
- Adenoids—nasopharyngeal tonsils.

SIGNS AND SYMPTOMS

- Sore throat.
- Pain with swallowing.
- May have whitish exudate on tonsils.
- Chronic tonsillitis:
  - Seven in past year.
  - Five in each of the past 2 years.
  - Three in each of the past 3 years.

TREATMENT

- <2–3 years old: Tonsillectomy is performed for obstructive sleep apnea (OSA) and recurrent/chronic infections.
- Large size alone is not an indication to remove tonsils.

ENLARGED ADENOIDS

DEFINITION

Nasopharyngeal lymphoid tissue hypertrophy.

SIGNS AND SYMPTOMS

- Mouth breathing.
- Persistent rhinitis.
- Snoring.
- Mucopurulent nasal discharge.

DIAGNOSIS

- Digital palpation and direct visualization.
- Indirect laryngoscopy.

TREATMENT

- Adenoidectomy:
  - Persistent mouth breathing.
  - Hyponasal speech.
  - Adenoid facies—open mouth, flattened/elongated midface, retracted upper lip, narrowed hard palate with crowded maxillary teeth.
  - Recurrent otitis media or nasopharyngitis.
- Tonsillectomy should not be performed routinely unless separate indication exists.

PERITONSILLAR ABSCESS (PTA)

DEFINITION

Walled-off infection occurring in the space between the superior pharyngeal constrictor muscle and the capsule of the palatine tonsils.

EXAM TIP

Tonsils and adenoids are part of Waldeyer's ring that circles the pharynx.

WARD TIP

It can be normal for tonsils to be relatively large during childhood.

WARD TIP

Enlarged adenoids is the MC nasal obstruction in children.
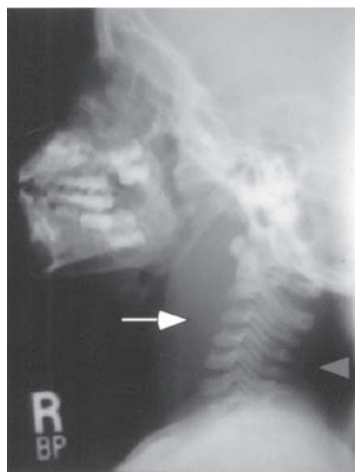
FIGURE 12-4. **Lateral radiograph of the soft tissue of the neck.** Note the large amount of prevertebral edema (solid arrow) and the collection of air (dashed arrow). Findings are consistent with retropharyngeal abscess. (Used with permission from Dr. Gregory J. Schears.)

ETIOLOGY

- GABHS.
- Anaerobes.

EPIDEMIOLOGY

Usually preadolescent.

SIGNS AND SYMPTOMS

- Preceded by acute tonsillopharyngitis.
- Severe throat pain, usually unilateral.
- Trismus.
- Refusal to swallow or speak.
- "Hot potato voice."
- Markedly swollen and inflamed tonsils.
- Uvula displaced to opposite side.

TREATMENT

- Antibiotics covering staph and strep. Typically, IV ampicillin—sulbactam or IV clindamycin. If there is no response to these initial antibiotics, add vancomycin.
- Needle aspiration or incision and drainage, followed by supportive care.

Retropharyngeal Abscess

DEFINITION

Potential space between the posterior pharyngeal wall and the prevertebral fascia. Commonly occurs in children <5 years old.

ETIOLOGY

Usually a complication of pharyngitis:
- GABHS.
- Oral anaerobes.
- S. *aureus.*

SIGNS AND SYMPTOMS

- Associated with recent URI.
- Sudden onset of high fever with difficulty in swallowing.
- Refusal of feeding due to dysphagia and odynophagia.
- Throat pain.
- Unwilling to hyper-extend the head.
- Toxicity is common.
- May cause meningismus—extension of the neck causes pain.

DIAGNOSIS

- Lateral neck x-ray: Widened pre-vertebral/retropharyngeal space (see Figure 12–4).
- May also see reversal of lordosis, the normal curvature of the cervical spine.

TREATMENT

- IV clindamycin or ampicillin-sulbactam.
- If airway compromised, immediate surgical drainage.

Asthma

A 5-year-old boy with a history of sleeping problems presents with a nonproductive nocturnal cough and shortness of breath and cough during exercise. *Think: Asthma.* Start on a trial of a bronchodilator, which is helpful in confirming the diagnosis by the demonstration of reversible airways obstruction ($\uparrow$ in forced expiratory volume in 1 second [FEV_1]). Asthma is an inflammatory disease. Diagnosis of asthma should be considered in the presence of recurrent wheezing in a child with a family history of asthma.

Definition

Respiratory hypersensitivity, inflammation, and reversible airway obstruction.

Etiology

Hyper-responsiveness to a variety of stimuli:
- Respiratory infection.
- Air pollutants.
- Allergens: Seasonal, dust, mold, animal dander.
- Foods.
- Exercise.
- Emotions.

Pathophysiology

- Bronchospasm (acute).
- Mucus production (acute).
- Inflammation and edema of the airway mucosa (chronic).
- Two types:
  - Extrinsic:
    - Immunologically mediated due to allergies.
    - Develop in childhood.
  - Intrinsic:
    - No identifiable cause, most likely stress, anxiety, exercise, quality of air, irritants.
    - Late onset.
    - Worsen with age.
- Underlying abnormalities in asthma include $\uparrow$ pulmonary vascular pressure, diffuse narrowing of airways, $\uparrow$ residual volume and functional residual capacity, and $\uparrow$ total ventilation maintaining normal or reduced PCO_2 despite $\uparrow$ dead space.

Signs and Symptoms

- Cough, wheezing, dyspnea, and tachypnea.
- $\uparrow$ work of breathing (retractions, use of accessory muscles, nasal flaring, abdominal breathing).
- $\downarrow$ breath sounds.
- Prolongation of expiratory phase.
- Acidosis and hypoxia may result from airway obstruction.
- See Table 12-5 for classification of severity.

Diagnosis

- Mostly a clinical diagnosis.
- Peak expiratory flow rate (PEFR): Is used to assess severity of an acute exacerbation.

WARD TIP

Asthma is the most common chronic lung disease in children.

EXAM TIP

It is important to ask for allergy history and family history of asthma.

WARD TIP

Lack of wheezing does not exclude asthma.

WARD TIP

In asthma there is cellular infiltration of mucosa by eosinophils, activated helper T cells, and mast cells.

WARD TIP

Asthma is the most common cause of cough in school-age children.

EXAM TIP

Before puberty, boys have a higher prevalence of asthma.

WARD TIP

URI is the most important triggering factor for patients with asthma of all ages.

TABLE 12-5. Asthma Severity Classification

CLASSIFYING SEVERITY OF ASTHMA EXACERBATIONS IN THE URGENT OR EMERGENCY CARE SETTING	
Mild	Dyspnea only with activity PEFR >70% predicted personal best
Moderate	Dyspnea interferes with or limits usual activity PEFR 40–69% predicted personal best
Severe	Dyspnea at rest, interferes with conversation PEFR <40% predicted personal best
Life threatening	Too dyspneic to speak PEFR <25% predicted personal best

PEFR, peak expiratory flow rate.

(Adapted with permission from National Asthma Education & Prevention Program Expert Panel Report 3: Guidelines for the Diagnosis & Management of Asthma NHLBI guidelines, *Summary Report* 2007: 54.)

> **WARD TIP**
>
> Classic trilogy of asthma:
> - Bronchospasm
> - Mucus production
> - Inflammation and edema of the airway mucosa

> **EXAM TIP**
>
> Respiratory drive is not inhibited in asthma.

> **WARD TIP**
>
> All wheezing is not caused by asthma; all asthmatics do not wheeze.

> **WARD TIP**
>
> Asthmatic patient in severe respiratory distress may not wheeze.

> **WARD TIP**
>
> O_2 is indicated for all asthmatics to keep O_2 saturation >95%.

> **WARD TIP**
>
> Low-dose daily inhaled corticosteroids are the first-line controller therapy for mild, persistent asthma.

- Maximal rate of airflow during forced exhalation after a maximal inhalation.
- Normal values depend on age and height:
    - Mild (80% of predicted).
    - Moderate (50–80% of predicted).
    - Severe (<50% of predicted).
- Spirometry—the preferred method of diagnosis of airflow obstruction.
    - Recommended >5 years old if asthma is suspected.
    - Measure forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV_1).
    - Airway obstruction present if $FEV_1 < 80\%$; $FEV_1/FVC < 85\%$.
- Chest x-ray will demonstrate hyperinflation and can be useful to look for pneumonia.
- Pulse oximetry may demonstrate hypoxia.
- ABG—hypoxia in severe exacerbations; hypercapnia suggestive of impending respiratory failure.
- Bloodwork should not be routinely ordered in the evaluation of asthma.

TREATMENT

Goals: Improve bronchodilation, avoid allergens, ↓ inflammation, educate patient.

First-Line Agents for Acute Exacerbations
1. Oxygen if O_2 saturation <92% on room air.
2. Inhaled β_2 agonist:
    - Albuterol (2.5 mg) (nebulized).
    - Short-acting/rescue medication—treats only symptoms, not underlying process.
    - Bronchial smooth-muscle relaxant in increase airflow.
    - Side effects: Tachycardia, tremors, hypokalemia.
3. Corticosteroids (sooner is better):
    - For treatment of chronic inflammation.
    - Oral prednisone (2 mg/kg, maximum 60 mg) or IV methylprednisolone 2 mg/kg (maximum 125 mg).
    - Contraindication: Active varicella or herpes infection.

4. Anticholinergic agents:
   - Ipratropium bromide (nebulized).
   - Act synergistically with albuterol.
   - Bind to cholinergic receptors in the medium and large airways.

Second-Line Agents
1. Magnesium sulfate—bronchodilation via direct effect on smooth muscle.
2. Epinephrine or terbutaline.
3. No role in acute asthma for theophylline; not recommended.

Others
1. Heliox—mixture of 60–70% helium and 30–40% oxygen:
   - ↓ work of breathing by improving laminar gas flow (nonintubated patient).
   - Improves oxygenation and ↓ peak airway pressure (intubated patients).
2. Mechanical ventilation indications:
   - Failure of maximal pharmacologic therapy.
   - Hypoxemia.
   - Hypercarbia.
   - Change in mental status.
   - Respiratory fatigue.
   - Respiratory failure.
3. Leukotriene modifiers: Used in long-term treatment of asthma.
   - Inflammatory mediators.
   - Improve lung function.
   - No role in acute asthma.
4. Cromolyn and nedocromil:
   - Effective in maintenance therapy.
   - Exercise-induced asthma.
   - May reduce dosage requirements of inhaled steroid.

Admit if:
- Respiratory failure requiring intubation.
- Status asthmaticus.
- Return ED visit in 24 hours.
- Complete lobar atelectasis.
- Pneumothorax/pneumomediastinum.
- Underlying cardiopulmonary disease.

STATUS ASTHMATICUS

DEFINITION
- Life-threatening form of asthma.
- Condition in which a progressively worsening attack is unresponsive to usual therapy.

SIGNS AND SYMPTOMS
Look for:
- Pulsus paradoxus >20 mm Hg.
- Hypotension, tachycardia.
- Cyanosis.
- One- to two-word dyspnea.
- Lethargy.
- Agitation.
- Retractions.
- Silent chest (no wheezes—poor air exchange).

EXAM TIP

Spirometry is the most important study in asthma.

WARD TIP

Long-acting β_2 agonist (salmeterol) should not be used for acute asthma exacerbation.

WARD TIP

Asthmatic child's ability to use inhaler correctly should be regularly assessed and should be used with a spacer to ensure most effective administration of dose.

EXAM TIP

Most important risk factor for morbidity is failure to diagnose asthma from recurrent wheezing.

WARD TIP

↑ white blood cell (WBC) count does not always signify infection in status asthmaticus.

WARD TIP

Ketamine is used for sedation/analgesia before intubating a child with asthma in respiratory failure due to its bronchodilatory properties.

Foreign Body Aspiration

👤 A 2-year-old boy is brought to the ED with a history of a choking or gagging episode, followed by a coughing spell. In the ED, he was noted to have wheezing. His respiratory rate is 24, and he has mild intercostal retractions. His babysitter found him playing in his room. *Think: Foreign body aspiration.*

👤 A previously healthy 12-year-old boy presented with cough for almost a year. He had a persistent dry cough during the day and night that was occasionally productive. His parents reported a history of pneumonia with consolidation of the right lower lobe on three different occasions in 6 months. On physical examination, no nasal congestion is noted. ↓ air entry and wheezing is noted on the right side of his chest. *Think: Foreign body aspiration.*

However, this classic triad (sudden onset of paroxysmal coughing, wheezing, and diminished breath sounds on the ipsilateral side) may not be present in all children with foreign body aspiration.

PATHOPHYSIOLOGY

Cough reflex usually protects against aspiration.

EPIDEMIOLOGY

- Twice as likely to occur in males, particularly 6-month-olds to 3-year-olds.
- Most common age: 1–2 years.

SIGNS AND SYMPTOMS

- Determined by nature of object, location, and degree of obstruction.
- Narrowest portion of the pediatric airway is at the cricoid ring.
- Foreign body in the upper airway: Respiratory distress with severe retractions and stridor.
- Foreign body in the lower airway (most foreign bodies lodge in the lower airways [80%]). Symptoms may be subtle.
- Initial respiratory symptoms may disappear for hours to weeks after incident.
- Vegetal/arachidic bronchitis due to vegetable (usually peanut) aspiration causes cough, high fever, and dyspnea.
- Most common aspirated foreign body: Peanut.
- Most common foreign body aspirations resulting in death: Balloons.
- Complications if object is not removed include pneumonitis/pneumonia, abscess, bronchiectasis, pulmonary hemorrhage, erosion, and perforation.

DIAGNOSIS/TREATMENT

Larynx
- Croupy cough; may have stridor, aphonia, hemoptysis, cyanosis.
- Lateral x-ray.
- Direct laryngoscopy—confirm diagnosis and remove object.

Trachea
- Stridor, audible slap, and palpable thud due to expiratory impaction.
- Chest x-ray (see Figure 12-5), bronchoscopy.

WARD TIP

Dehydration may be present in status asthmaticus, but over hydration should be avoided (risk for syndrome of inappropriate antidiuretic hormone secretion [SIADH]).

WARD TIP

Prevention is key! Keep small food and objects away from young children.

WARD TIP

Caution! Do not try to remove foreign bodies causing partial upper airway obstruction because these attempts may result in complete glottic obstruction.

WARD TIP

Foreign Body Aspiration
- Most are located in the bronchi.
- Toddlers: R = L mainstem
- Adults: R mainstem predominates

F I G U R E   1 2 - 5 .   Radiograph of lateral soft tissue of the neck demonstrates a foreign body (nail) in the pharynx. (Used with permission from Dr. Gregory J. Schears.)

Bronchi
- Initial choking, gagging, wheezing, coughing.
- Latent period with some coughing, wheezing, possible hemoptysis, recurrent lobar pneumonia, or intractable asthma.
- Tracheal shift, ↓ breath sounds.
- Midline obstruction can cause severe dyspnea or asphyxia.
- → chronic bronchopulmonary disease if not treated.
- Direct bronchoscopic visualization (Figure 12-6).
- Antibiotics for secondary infection if prolonged exposure.
- Emergency treatment of local upper airway obstruction if necessary.
- If the child can cough and verbalize:
  - Provide supplemental oxygen.
  - Maintain position of comfort.
  - Immediate consultation with ENT and anesthesia.
- If the child cannot cough or verbalize, initiate basic life support.

F I G U R E   1 2 - 6 .   Foreign body (peanut) in the right mainstem bronchus visualized by bronchoscopy. Foreign bodies tend to lodge most commonly in the right mainstem bronchus due to the larger anatomic angle that makes traveling down right mainstem easier. (Used with permission from Dr. Gregory J. Schears.)

Tracheoesophageal Fistula (TEF)

DEFINITION

Connection between the trachea and esophagus (see Figure 12-7).

ETIOLOGY

- Congenital.
- Acquired.

SIGNS AND SYMPTOMS

- Suspect esophageal atresia.
- Maternal polyhydramnios.
- Inability to pass catheter into stomach.
- ↑ oral secretions—drooling.
- Choking, cyanosis, or coughing with an attempt to feed.
- Tachypnea.

DIAGNOSIS

- X-ray: Radiopaque feeding tube passes no further than proximal esophagus.
- Barium swallow: Aspiration of barium into the tracheobronchial tree.
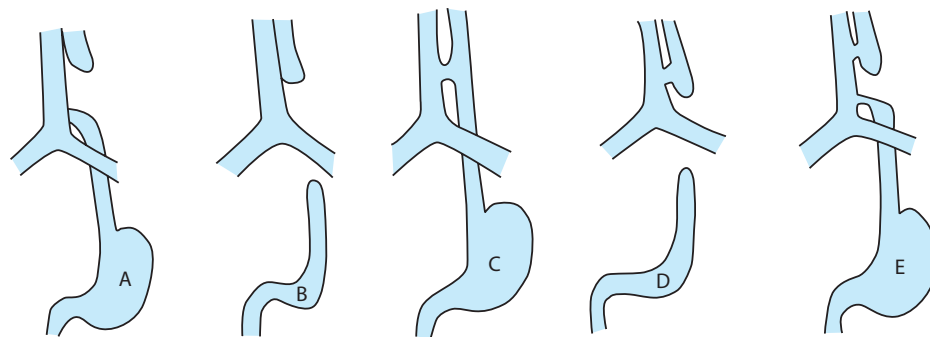
FIGURE 12-7. **Types of tracheoesophageal fistulas (TEFs).** Type A, esophageal atresia (EA) with distal TEF (87%). Type B, isolated EA. Type C, isolated TEF. Type D, EA with proximal TEF. Type E, EA with double TEF.

TREATMENT

Esophageal atresia is a surgical emergency—ligation of the fistula is performed.

Laryngomalacia

DEFINITION

- Collapse of supraglottic structures during inspiration.
- Disproportionately small and soft larynx.

SIGNS AND SYMPTOMS

- Usually begins within first month.
- Noisy breathing, snoring.
- "Wet" inspiratory stridor most frequent cause of stridor in children.
- Symptoms can be intermittent.
- Hoarseness or aphonia (laryngeal crow).
- Feeding difficulty; gastroesophageal reflux, laryngoesophageal reflux.
- Symptoms worse when crying or lying on back.

DIAGNOSIS

- Flexible fiberoptic laryngoscopy.
- Collapse of laryngeal structures during inspiration especially arytenoid cartilages.

TREATMENT

- Reassurance.
- No specific therapy required.
- Usually resolves spontaneously by 18 months.
- Surgery is rare and only done if severe.

Congenital Lobar Emphysema (Infantile Lobar Emphysema)

DEFINITION

Developmental anomaly of the lower respiratory tract that is characterized by hyperinflation of one or more of the pulmonary lobes.

EPIDEMIOLOGY

- Most common congenital lung lesion.
- More common in males (3:1)

PATHOPHYSIOLOGY

No significant parenchymal destruction.

SIGNS AND SYMPTOMS

- Normal at birth.
- Cough, wheezing, dyspnea, and cyanosis within a few days.
- Decreased breath sounds and hyper-resonant to percussion over involved lobe.

DIAGNOSIS

- Chest x-ray:
    - Distention of the affected lobe.
    - Can see compressive atelectasis of contralateral lung.
    - Radiolucency.
    - Mediastinal shift to opposite side.
    - Flattened diaphragm.

TREATMENT

Lobectomy.

Cystic Adenomatoid Malformation

DEFINITION

- Also called congenital pulmonary airway malformation (CPAM).
- Developmental anomaly of the lower respiratory tract.
- Excessive overgrowth of bronchioles.
- ↑ in terminal respiratory structure.
- Hamartomatous lesions in tracheal, bronchial, bronchiolar, and alveolar tissues.

EPIDEMIOLOGY

Second most common congenital lung lesion.

SIGNS AND SYMPTOMS

- Neonatal respiratory distress.
- Recurrent pneumonia in same location.
- Pneumothorax.
- May be confused with diaphragmatic hernia in neonatal period.
- Can be asymptomatic.

DIAGNOSIS

- Chest x-ray (posteroanterior [PA], lateral, and decubitus).
- Cystic mass (multiple grapelike sacs) and mediastinal shift.
- Air-fluid level.
- CT scan shows small and large air- or fluid-filled cysts.

TREATMENT

Surgical excision of affected lobe.

WARD TIP

Both CLE and CAM can be diagnosed prenatally by ultrasound.

WARD TIP

Disorders of HOXB5 gene have been noted with CAM.

WARD TIP

In patients with cystic adenomatoid malformation, avoid attempted aspiration or chest tube placement, as there is the risk of spreading infection.

EXAM TIP

Cystic adenomatoid malformation ↑ the risk for pulmonary neoplasia.

NOTES

Cardiovascular Disease

Murmurs

NORMAL HEART SOUNDS

- S1, produced by closure of the tricuspid and mitral valves, may split.
- S2, produced by closure of the aortic (A2) and pulmonic (P2) valves, normally splits with respiration.
- S3 can represent normal, rapid ventricular refilling.
- P2 should be soft after infancy.

EPIDEMIOLOGY

- Up to 90% of children have a murmur at some point in their lives.
- Two to seven percent of murmurs in children represent pathology.

DESCRIPTION AND GRADING

Murmurs are graded for intensity on a six-point system:
- **Grade I:** Very soft murmur detected only after very careful auscultation.
- **Grade II:** Soft murmur that is readily heard but faint, roughly equal to S1/S2.
- **Grade III:** Moderately intense murmur not associated with a palpable precordial thrill, louder than S1 or S2.
- **Grade IV:** Loud murmur; a palpable precordial thrill is not present or is intermittent.
- **Grade V:** Loud murmur associated with a palpable precordial thrill.
- **Grade VI:** Loud murmur associated with a palpable precordial thrill. It can be heard even when the stethoscope is lifted slightly from the chest.

SITES OF AUSCULTATION

See Figure 13-1 to correlate the following points:
1. **Carotid arteries.** Common murmurs heard here: Carotid bruit, aortic stenosis (AS).
2. **Aortic valve.** Right upper sternal border. Common murmurs: AS. Valvular stenosis will often have an ejection click.
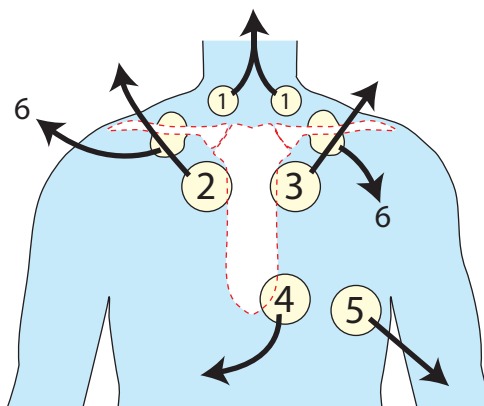
FIGURE 13-1. Sites of auscultation.

WARD TIP

Murmur grading is usually written as "Grade [#]/6."

3. **Pulmonic valve.** Left upper sternal border. Common murmurs: Pulmonary valve stenosis, atrial septal defect (ASD), pulmonary flow murmur, pulmonary artery stenosis, patent ductus arteriosus (PDA).
4. **Tricuspid valve.** Left lower sternal border. Common murmurs: Ventricular septal defect (VSD), Still's murmur, hypertrophic obstructive cardiomyopathy (HOCM), tricuspid regurgitation, endocardial cushion defect.
5. **Mitral valve.** Apex. Common murmurs: Mitral regurgitation, mitral valve prolapse, Still's murmur.
6. This site correlates with areas of **venous confluence.** Common murmurs: Venous hum or subclavian bruit.

ACCENTUATION MANEUVERS

Various positions and activities can diminish and intensify a murmur (see Table 13-1). The following section also reiterates the positions that aid in diagnosing innocent murmurs.

> **EXAM TIP**
>
> HOCM (hypertrophic obstructive cardiomyopathy) murmur will get louder with decreased preload (Valsalva maneuvers) and subaortic stenosis get softer with decreasing preload (such as squatting or any Valsalva maneuver).

TABLE 13-1. Accentuation Maneuvers for Pathologic Murmurs

MURMUR	INCREASED WITH	DECREASED WITH
Patent ductus arteriosus	Supination	
Atrial septal defect	(Valsalva can cause a temporary middiastolic murmur)	(Occasional crescendo-decrescendo systolic ejection murmur heard with ASD will not ↓ in intensity with the Valsalva maneuver like the pulmonary murmur)
Aortic stenosis	Valsalva release, sudden squatting, passive leg raising	Valsalva maneuver, handgrip, standing
Subaortic stenosis	Valsalva maneuver, standing	
Hypertrophic obstructive cardiomyopathy	Valsalva maneuver, standing	Handgrip, squatting, leg elevation
Mitral valve prolapse	(Click and murmur occur earlier and the murmur is longer [not louder] with inspiration, when upright, and during the Valsalva maneuver)	
Mitral regurgitation	Sudden squatting, isometric handgrip	Valsalva maneuver, standing
Pulmonic stenosis	Valsalva release	Valsalva maneuver, expiration
Tricuspid regurgitation	Inspiration, passive leg raising	Expiration
Aortic regurgitation	Sudden squatting, isometric handgrip	
Mitral stenosis	Exercise, left lateral position, isometric handgrip, coughing	
Tricuspid stenosis	Inspiration, passive leg raising	

T A B L E   1 3 - 2 .   Innocent Murmurs

Murmur	Cause	Epidemiology	Location	Sound	Characteristics
Pulmonary flow murmur	Turbulent flow through a normal pulmonary valve	Most common between 8 and 14 years	Mid to upper left sternal border	Midfrequency, crescendo–decrescendo, systolic	Louder when patient is supine than upright
Still's (vibratory) murmur	Possibly turbulent flow in the left ventricular outflow tract region	Most common between 3 and 6 years; uncommon < 2 years	Lower left sternal border	Musical or vibratory with midsystolic accentuation	Louder supine, may disappear with Valsalva, softer during inspiration
Venous hum	Turbulent flow of systemic venous return in the jugular veins and superior vena cava	Most common between 3 and 6 years	Infra- and supraclavicular, base of neck	High frequency, best heard with diaphragm, during systole and diastole	More prominent on right than left, can be accentuated or eliminated with head position, disappears supine or digital compression of jugular vein
Carotid bruit or subclavian bruit	Turbulent flow from abrupt transition from large-bore aorta to smaller carotid and brachiocephalic arteries	Any age	Over carotid arteries with radiation to head	Systolic	Rarely, a faint thrill is palpable over the artery
Physiologic pulmonary branch stenosis (PPS)	Turbulent flow as blood enters right and left pulmonary arteries that are relatively hypoplastic at birth due to patent ductus arteriosus predominance	Newborns, especially low birth weight (usually disappears by 3–6 months)	Upper left sternal border, axillae, and back	Crescendo-decrescendo, systolic	Louder supine
Patent ductus arteriosus	Turbulent flow as blood is shunted left to right from the aorta to the pulmonary artery	Can be innocent in newborns, abnormal if persists	Upper left sternal border	Continuous, machinery-like, louder in systole	

Innocent Murmurs

- Typically from turbulent blood flow rather than structural disease, and do not have hemodynamic significance.
- Common to all innocent murmurs are:
    - Absence of structural heart defects.
    - Normal heart sounds (S1, S2) with normal peripheral pulses.

- Normal chest radiographs and electrocardiogram (ECG).
- Asymptomatic.
- Usually systolic and graded less than III.
- **No association with cardiovascular disease.**
- **Accentuated in high-output states (fever and anemia).**
- **Pulmonary flow murmurs** and **Still's murmurs** can all be heard best when the patient is supine versus upright.
- A Still's murmur may disappear with the Valsalva maneuver.
- Pulmonary flow murmurs are augmented by full exhalation, diminished by inhalation.
- **Venous hum** is continuous, disappears in the supine position, and can be eliminated with digital compression of the jugular vein.
- See Table 13-2.

Pathologic Murmurs

See Table 13-1.

Interpretation of Pediatric ECGs

- Always approach an ECG systematically:
  1. Rate: Measure atrial and ventricular rates.
  2. Rhythm: Define the rhythm (sinus, or other).
  3. Axes: Measure the axes of the P waves, QRS complexes, and T waves.
  4. Intervals: Measure the P-R interval, QRS duration, and Q-T interval.
  5. Morphology: Look for abnormalities of wave patterns and voltages.
- **Pediatric considerations:**
  - The interpretation is age dependent.
  - Heart rate varies with age—higher in infants and children (see Table 13-3).
  - The PR interval and QRS duration are shorter in children.
  - QT_c is longer in infants than in older children (QT interval varies with heart rate).

ECG PAPER

- Speed = 25 mm/s.
- Small box = 0.04 second = 1 mm.
- Large box = 0.20 second = 5 mm.

ATRIAL RATE

- If P wave number is greater than QRS complex number, an atrial dysrhythmia may be present.
- Premature atrial contractions (PACs) are common in infancy.

VENTRICULAR RATE

- Count number of QRS complexes in typical 6-second ECG and multiply by 10.
- If irregular or fast rate, count R-R cycles in six large boxes, then multiply by 50.

TABLE 13-3. Heart Rate by Age

AGE	NORMAL RANGE (AVERAGE)
< 1 day	93–154 bpm (123)
1–2 days	91–159 bpm (123)
3–6 days	91–166 bpm (129)
1–3 weeks	107–182 bpm (148)
1–2 months	121–179 bpm (149)
3–5 months	106–186 bpm (141)
6–11 months	109–169 bpm (134)
1–2 years	89–151 bpm (119)
3–4 years	73–137 bpm (108)
5–7 years	65–133 bpm (100)
8–11 years	62–130 bpm (91)
12–15 years	80–119 bpm (85)
> 16 years	60–100 bpm

BRADYCARDIA

- Many causes: Sleep, sedation, vagal stimulation (stooling, cough, or gag), hypothyroid, hyperkalemia, hypothermia, **hypoxia,** athletic heart, second- or third-degree atrioventricular (AV) block, junctional rhythm, ↑ intracranial pressure, medicine (i.e., digitalis, β blockers).
- Hypoxemia is the most common cause of bradycardia in children.

TACHYCARDIA

Found in fever, anxiety, pain, hypovolemia, sepsis, congestive heart failure (CHF), hyperthyroidism, supraventricular tachycardia (SVT), ventricular tachycardia, atrial flutter and fibrillation, medicine (i.e., theophylline, stimulants).

RHYTHM

Check for sinus rhythm (depolarization originating from the sinus node):
- Verify a P wave before every QRS complex, and a QRS complex after every P wave.
- Examine morphology: All P waves should look the same.
- Normal P wave axis (0° to +90°) with upright P waves in leads I and aVF.

- Normal P wave:
    - <0.10 second in children (1/2 big box).
    - <0.08 second in infant (2 small boxes).

SINUS ARRHYTHMIA

Normal variation in heart rate due to inspiration and expiration, commonly seen in childhood.

ABNORMAL RHYTHMS

Premature Atrial Contraction (PAC)

- Preceded by a P wave, followed by a normal QRS.
- No hemodynamic significance.

Premature Ventricular Contraction (PVC)

- Premature and wide QRS, no P wave, T wave opposite to QRS.
- May be normal if they are uniform and ↓ with exercise.
- Must evaluate further if there are runs of PVCs or they occur regularly.

Atrial Flutter

- A rapid atrial rate (∼300 bpm) in a sawtooth pattern, with a varying ventricular rate depending on degree of block (i.e., 2:1, 3:1).
- Normal QRS.
- Usually suggests significant pathology (atrial enlargement).

Atrial Fibrillation

- Very fast atrial rate (350–600 bpm) with an irregularly irregular ventricular response.
- No P waves; normal QRS.
- Usually suggests significant pathology.

Ventricular Tachycardia

- Series of 3+ PVCs with a heart rate between 120 and 200 bpm.
- Wide, unusually shaped QRS complexes, indicating depolarization traveling outside of the His-Purkinje system.
- T waves in opposite direction of QRS complex.
- Usually suggests significant pathology, and should be terminated electrically (if unstable) or medically (if stable).

Ventricular Fibrillation

- Very irregular QRS complexes without P waves.
- The rate is rapid and irregular.
- This is a terminal arrhythmia because the heart cannot fill and maintain effective circulation; should be terminated with an AED.

Supraventricular Tachycardia (SVT)

- Narrow QRS complex, no variability in R-R interval, without discernible P waves.
- Sudden onset and resolution spontaneously or with Valsalva maneuvers.
- Reentrant tachycardia that utilizes the AV node in reentrant circuit.
- Usually associated with structurally normal hearts.
- SVT with aberrant conduction producing wide QRS may look like V-tach.

AXIS

QRS Axis

- Examine leads I and aVF.
  - If net positive deflection in lead I, the axis range is between $+90°$ and $-90°$.
  - If net positive deflection in lead aVF, the QRS is also between $0°$ and $+180°$.
- Superimpose the ranges. Region of overlap is where quadrant QRS lies in.
- If positive (upward) in I and aVF, axis is normal.

Abnormal Axes

- Right-axis deviation (RAD): Severe pulmonary stenosis with right ventricular hypertrophy (RVH), pulmonary hypertension (HTN), conduction disturbances (RBBB).
- Left-axis deviation (LAD) with RVH is highly suggestive of AV canal. Consider especially with Down syndrome.
- Mild LAD with left ventricular hypertrophy (LVH) in a cyanotic infant suggests tricuspid atresia.

P Axis

- Normal is [+] deflection in II, [−] in aVR. This defines sinus rhythm and normally related atria (atrial situs solitus).
- A P axis $>+90°$ suggests atrial inversion or misplaced leads.

ABNORMAL WAVE PATTERNS AND VOLTAGES

Abnormal Q waves

- Q waves of new onset or of ↑ duration may represent myocardial infarction (MI).
- Causes of ischemia and infarction: Anomalous origin of left coronary artery from pulmonary artery, coronary artery aneurysm and thrombosis in Kawasaki disease, asphyxia, cardiomyopathy, severe aortic stenosis, myocarditis, cocaine use.
- A deep, wide Q wave in aVL is a marker for LV infarction. Suspect anomalous origin of left coronary artery, particularly in a child <2 months old.

ST Segment

- End of S to beginning of T.
- Causes of ST displacement: Pericarditis, cor pulmonale, pneumopericardium, head injury, pneumothorax.
- Elevation may result from ischemia or pericarditis.

T wave

- Peaked, pointed T waves occur with hyperkalemia, LVH, and head injury.
- Flattened T waves are seen in hypokalemia and hypothyroidism.

Right Atrial Enlargement

- Peaked P waves (leads II and V1).
- Causes include cor pulmonale (pulmonary hypertension, RVH), anomalous pulmonary venous connection, large ASD, Ebstein's anomaly.

Left Atrial Enlargement

- Wide P wave (notched in II, deep terminal inversion in V1).
- Causes include VSD, PDA, mitral stenosis.
- The wider and deeper the terminal component, the more severe the enlargement.

Right Ventricular Hypertrophy (RVH)

- Right-axis deviation alone is not enough as a criterion for RVH; many other criteria exist.
- Causes include ASD, TAPVR, pulmonary stenosis, tetralogy of Fallot (TOF), large VSD with pulmonary HTN, coarctation in the newborn.

Left Ventricular Hypertrophy (LVH)

- Excessive LAD supports LVH but is not sufficient to make the diagnosis.
- Causes include VSD, PDA, anemia, complete AV block, aortic stenosis, systemic HTN, obstructive and nonobstructive hypertrophic cardiomyopathies.

Combined Ventricular Hypertrophy (CVH)

- If criteria for RVH exist and left ventricular forces exceed normal mean values for age, the patient has CVH. If LVH is present, similar reasoning may apply to the diagnosis of RVH.
- Causes include left-to-right shunts with pulmonary HTN (large VSD) and complex structural heart disease.
- Cannot diagnose ventricular hypertrophy in the absence of normal conduction (RBBB).

Decreased QRS Voltage

- <5 mm in limb leads.
- Causes include pericardial effusion, pericarditis, hypothyroidism.
- Sometimes normal newborns have ↓ voltages—not a concern.

Wolff-Parkinson-White Syndrome

- Ventricular preexcitation via accessory conduction pathway through the Bundle of Kent.
- Accessory pathway conducts more rapidly (than the normal AV node) but takes longer to recover.
- Shortened PR interval, widened QRS caused by slurred upstroke → **delta wave**.
- Associated with Ebstein's anomaly.
- ↑ risk of SVT and sudden death.
- **Treatment:** Surgical ablation of accessory pathway.

Basics of Echocardiography

- There are four basic cross-sectional views taken of the heart with **transthoracic echocardiography (TTE):** Parasternal (long and short axis), apical, subcostal (taken in the midline below the xiphoid process), suprasternal.
- **Transesophageal echocardiography** employs a transducer introduced down the esophagus for enhanced imaging during cardiac surgery or catheterization.

EXAM TIP

Causes of Sudden Cardiac Deaths in Young Athlete:
- Hypertrophic cardiomyopathy (HOCM)
- Arrhythmogenic right ventricular cardiomyopathy
- Congenital coronary artery anomalies
- Aortic rupture with Marfan syndrome
- Wolff-Parkinson-White syndrome
- Congenital long QT syndrome.

WARD TIP

In infants and children, coronary arteries can be evaluated nicely using TTE.

2-D ECHOCARDIOGRAPHY

Cross-sectional images of the heart are seen via this method to assess structures including inflow and outflow tracts, valves, ascending and descending aorta, pulmonary arteries and veins, atria, ventricles, and septa.

COLOR-FLOW DOPPLER ECHOCARDIOGRAPHY

- Blood flow and direction can be seen via this method.
  - Red indicates blood flowing toward the transducer.
  - Blue indicates blood flowing away from the transducer.

M Mode Echocardiography

- In this mode, the information from one scan point is measured over time.
- Motion creates a graph of depth of structures (i.e., valves, ventricular wall, etc.) versus time.
- This modality is used to determine cardiac chamber dimension, valve annuli size, fractional shortening and ejection fraction, left ventricular mass.

Fetal Echocardiography

- For the prenatal diagnosis of congenital heart diseases.
- Allows for improved counseling and better understanding of the postnatal prognosis.
- Screen at >16 weeks.
- Indications:
  - Fetal:
    - Abnormal screening obstetric ultrasound.
    - Extracardiac anomalies.
    - Chromosomal abnormalities.
    - ↑ first-trimester nuchal translucency measurement (trisomy 21 and Turner syndrome).
  - Maternal (diabetes, phenylketonuria).

Interpretation of Pediatric Chest X-Rays

HEART SIZE

Cardiothoracic ratio:
- Measure largest width of the heart and divide by the largest diameter of the chest. A normal ratio is <0.6.
- The CXR must have a good inspiratory effort. For this reason, newborns and infants are difficult to evaluate by this method.
- Cardiomegaly on CXR is most suggestive of volume overload.

PULMONARY VASCULAR MARKINGS

Increased Pulmonary Vascular Markings

- Noted by the visualization of pulmonary vasculature in the lateral one-third of the lung field. Represents increased blood flow through the pulmonary vasculature.
- In an **acyanotic** child this could be caused by ASD, VSD, PDA, endocardial cushion defect (**left to right shunting**).
- In a **cyanotic** child this could be from transposition of the great arteries, TAPVR, hypoplastic left heart syndrome, persistent truncus arteriosus, or single ventricle (**right to left shunting**).

EXAM TIP

In newborns and small infants, the upper aspects of the heart are obscured by a large "boat sail–shaped" opacity—the thymus. This organ will involute after puberty. It is often not seen in premature newborns.

Decreased Pulmonary Vascular Markings

- The lung fields are dark, with small vessels.
- Seen in conditions limiting blood flow through the pulmonary vasculature, such as pulmonary stenosis and atresia, tricuspid stenosis and atresia, and tetralogy of Fallot, as well as some conditions causing pulmonary hypertension.

Pulmonary Venous Congestion

- Manifested as hazy lung fields.
- Kerley B lines are often present.
- Caused by LV failure or obstruction of the pulmonary veins, causing pulmonary venous hypertension.
- Seen in mitral stenosis, TAPVR, hypoplastic left heart syndrome, or any left-sided obstructive lesion with heart failure.

> ✋ **WARD TIP**
>
> Conditions which cause right to left shunts lead to cyanosis. Conditions which cause left to right shunting lead to CHF and pulmonary vascular congestion.

ABNORMAL CARDIAC SILHOUETTES

Tetralogy of Fallot

- A "boot-shaped" heart with ↓ pulmonary vascular markings is sometimes seen. The boot is due to the hypoplastic main pulmonary artery.
- RVH is noted.

TRANSPOSITION OF THE GREAT ARTERIES

- An "egg-shaped" heart is sometimes seen.
- The narrow superior aspect of the cardiac silhouette is due to the absence of the thymus and the irregular relationship of the great arteries.

Total Anomalous Pulmonary Venous Return

- A "snowman" shape is sometimes seen.
- The left vertical vein, left innominate (brachiocephalic) vein, and dilated superior vena cava create the "snowman's" head.

Rheumatic Fever

DEFINITION

- Rheumatic fever (RF) is a delayed immunologic sequela of a previous group A streptococcal infection of the pharynx.
- Cutaneous streptococcal infection is a precursor of glomerulonephritis, but not rheumatic fever.
- Affects the brain, heart, joints, and skin.

EPIDEMIOLOGY

- Incidence: Close to ½ million cases per year worldwide. Although an uncommon disease in the United States, small outbreaks occur in various regions.
- Peak age range: 5–15 years.
- ↑ risk with a positive family history of rheumatic fever.
- Risk of RF after untreated strep pharyngitis is 1–3%. Patients with the infection <3 weeks have a 0.3% risk.
- Follows pharyngitis by 1–5 weeks (average: 3 weeks).
- Rate of recurrent RF with subsequent strep infection may approach 65%.
- Recurrence rate ↓ to <10% over 10 years.

CLINICAL FEATURES

Carditis
- Incidence: 50–70% of patients.
- Clinical presentation:
  - Tachycardia is common.
  - Heart murmur, most commonly due to valvulitis of the following (in order of decreasing frequency):
    - Mitral valve regurgitation.
    - Aortic valve regurgitation.
    - Tricuspid valve regurgitation.
  - Pericarditis (may hear a friction rub).
  - Cardiomegaly.
  - CHF (may hear a gallop).

Arthritis
- Affects 35–65% of patients, and is usually the first symptom of ARF.
- Usually affects the large joints, but can affect the spine and cranial joints.
- Migratory in nature, affecting new joints as other affected joints resolve.
- Joints are red, warm, swollen, and very tender, particularly if moved.
- Responds well to aspirin therapy.
- Duration is usually <1 month, even without treatment.

Chorea
- Incidence: 10–30% of patients.
- Characteristics:
  - Initial emotional lability: Behaviors characteristic of attention deficit/hyperactivity disorder (ADHD) and obsessive-compulsive disorder (OCD) have been noted to precede the movement disorder.
  - Loss of motor coordination.
  - Spontaneous, purposeless movement.
  - Motor weakness.
- Has a longer latent period than other symptoms, presenting 1–8 months after GAS infection; then lasts for months, before slowly diminishing.

Erythema Marginatum
- Incidence: <10% of patients.
- Pink, erythematous, nonpruritic macular rash.
- Often has a clear center and serpiginous outline.
- Evanescent and migratory.
- Disappears when cold, reappears when warm.
- Found primarily on the trunk and proximal extremities.

Subcutaneous Nodules
- Incidence: 2–10% of patients.
- Hard, painless, small (0.5–1 cm) swellings over bony prominences, primarily the extensor tendons of the hand.
- Can also be found on the scalp and along the spine.
- Not transient, lasting for weeks.

DIAGNOSIS

- To diagnose acute rheumatic fever (ARF) you must fulfill the following combination of the Jones criteria:
  - Two major manifestations *or*
  - One major and two minor manifestations.
- Aschoff bodies (found in atrial myocardium) are diagnostic.

- Streptococcal antibody tests are the most reliable evidence of preceding group A strep infection.
- Antistreptolysin O (ASO) titer is the most commonly used. It is elevated in 80% of patients with ARF and 20% of normal individuals.
- Other antibody tests exist (antihyaluronidase, antistreptokinase, anti-deoxyribonuclease B) wherein at least one will be positive in 95% of patients with ARF.
- Positive throat cultures and "rapid strep tests" are less reliable because they do not differentiate acute infection versus chronic carrier state.

TREATMENT

- Upon diagnosis, the patient should receive aspirin to reduce fever and alleviate arthritis symptoms, and oral penicillin V for 10 days or penicillin G IM, single dose to eradicate the streptococci.
- Patients allergic to penicillin can receive 5 days of azithromycin.
- Prophylaxis should be initiated:
    - Benzathine penicillin G IM every 3–4 weeks *or*
    - Penicillin PO three times per day *or*
    - Sulfadiazine PO once per day.
- Length of prophylaxis is undetermined but often advocated at least throughout adolescence, if not indefinitely. Obviously, compliance becomes a difficult issue.
- Seventy-five percent of patients recover within 6 weeks, and less than 5% are symptomatic beyond 6 months. Seventy percent of those with carditis recover without permanent cardiac damage.

Endocarditis

> A 6-year-old girl with PDA develops fever and anorexia. Her Hgb is 9; she has hematuria, ↑ ESR, positive rheumatoid factor (RF), and immune complexes are present. *Think: Bacterial endocarditis.*
> Predisposition: Congenital heart disease.
> Greatest risk factor: Systemic-pulmonary arterial communications such as patent ductus arteriosus.
> Possible additional findings: Chronic anemia, microscopic hematuria, elevated ESR, positive rheumatoid factor, circulating immune complexes, and low complement levels *are* all may be present in infective endocarditis.

ETIOLOGY

- **α-Hemolytic streptococci** are most common (70%), *Streptococcus pneumoniae* and *Streptococcus viridans*.
- **Staphylococcus aureus** is also common, accounting for 20% of cases.
- If felt to be secondary to cardiac surgery complications, *Staphylococcus epidermidis*, gram-negative bacilli (HACEK organisms), and fungi should be considered.
- Culture-negative endocarditis: *Think: Coxiella burnetii* or *Bartonella*.
- Most endocarditis in children is left-sided.

PATHOPHYSIOLOGY

Turbulent blood flow across an abnormal valve. Valves can be congenitally abnormal (bicuspid or atretic), damaged by rheumatic fever, have an acquired valvular lesion, or be a prosthetic replacement valve.
Any cardiac defect can also cause turbulent blood flow across a valve.

WARD TIP

Jones Criteria (Modified)
2 major or 1 major + 2 minor
Major—J♥NES:
- **J**oints—polyarthritis
- ♥—carditis
- **N**odules, subcutaneous
- **E**rythema marginatum
- **S**ydenham's chorea

Minor:
- Arthralgia
- Fever
- Elevated erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP)
- Prolonged P-R interval

Plus:
- Laboratory evidence of antecedent group A strep infection (ASO titer)

WARD TIP

Erythema marginatum is never found on the face.

WARD TIP

Subcutaneous nodules are also found in connective tissue diseases such as systemic lupus erythematosus (SLE) and rheumatoid arthritis.

WARD TIP

Subcutaneous nodules in rheumatic fever have a significant association with carditis. They are painless and palpable nodules, usually found on extensor surfaces and over bony prominences.

SIGNS AND SYMPTOMS

- Fever is most common.
- New or changing heart murmur.
- Chest pain, dyspnea, arthralgia, myalgia, headache.
- Embolic phenomena:
  - Hematuria with red cell casts.
  - Acute brain ischemia (embolic stroke caused by septic emboli).
  - Roth spots, splinter hemorrhages, Osler nodes, Janeway lesions (less common in children).

PREDISPOSING CONDITIONS

- High risk:
  - Prosthetic cardiac valves.
  - Previous bacterial endocarditis (due to scar formation on valve).
  - Congenital heart disease—complex cyanotic types.
  - Surgical pulmonary-systemic shunts, done to correct cyanotic heart conditions.
- Moderate risk:
  - Acquired valvular dysfunction, which can occur with radiation therapy or lupus.
    - Rheumatic heart disease, Libman-Sacks valve, antiphospholipid syndrome–associated valve disease.
    - Libman-Sacks valve: Nonbacterial endocarditis associated with lupus.
  - Hypertrophic cardiomyopathy.
  - Complicated mitral valve prolapse (valvular regurgitation, thickened valve leaflets).

DIAGNOSIS

- Multiple (recommend at least 3) sets of blood cultures over 48 hours from different sites for the diagnostic work-up.
- Most common findings:
  - Positive blood cultures.
  - Elevated ESR.
  - Hematuria.
  - Anemia.
- Echocardiographic evidence of vegetations or thrombi is diagnostic.

TREATMENT

- Four to eight weeks of organism-specific IV antibiotic therapy.
- Surgery is necessary when endocarditis is refractory to medical treatment. Also considered in cases of prosthetic valves, fungal endocarditis, and hemodynamic compromise.
- Antibiotic prophylaxis prior to dental procedures is necessary for children with structural heart disease and other predisposing conditions.
- Oral amoxicillin is given. For patient with PCN allergy, use Clindamycin.

PROPHYLAXIS RECOMMENDATIONS

- Prophylaxis is recommended with:
  - Most dental and periodontal procedures.
  - Surgeries:
    - Tonsillectomy or adenoidectomy.
    - Surgery involving GI or upper respiratory mucosa.
    - Gallbladder surgery.

- Urinary tract surgery.
- Incision and drainage of infected tissues.
- Rigid bronchoscopy.
- Catheterization in setting of urinary tract infection, cystoscopy, urethral dilation.
- Prophylaxis is *not* usually recommended with:
  - Shedding of primary teeth.
  - Tympanostomy tube insertion.
  - Endotracheal tube insertion.
  - Bronchoscopy with flexible bronchoscope.
  - Transesophageal echo.
  - GI endoscopy, with or without biopsy (prophylaxis for high-risk patients).
  - Circumcision.

Myocarditis

ETIOLOGY

- Most often caused by viruses. Coxsackieviruses and echoviruses are most common. Recent evidence suggests adenovirus as a common etiology.
- Immune-mediated diseases (e.g., ARF, Kawasaki disease).
- Toxic ingestions, like alcohol, amphetamines, anthracyclines, and some antipsychotics like clozapine.

EPIDEMIOLOGY

Clinically recognizable myocarditis is rare in the United States. Chagas disease is a common cause in developing countries.

PATHOPHYSIOLOGY

Inflammatory cardiomyopathy, inflammation of the heart muscle, caused by an underlying insult such as a viral infection can cause dilated cardiomyopathy and heart failure.

SIGNS AND SYMPTOMS

- Presentation depends on the degree of myocardial injury, ranges from asymptomatic to fulminant CHF.
- Common symptoms are fever, dyspnea, upper respiratory symptoms, vomiting, and lethargy.
- CHF should be considered if patient is tachycardic and tachypneic and has a gallop on auscultation.

DIAGNOSIS

- ECG findings: Sinus tachycardia, low voltages, non-specific S-T changes, prolonged QT interval, premature beats.
- Radiology: Chest radiographs will show cardiomegaly.
- Echocardiography: Chamber enlargement is present with impaired ventricular function.

TREATMENT

- First, treat the underlying cause (i.e., antibiotics if bacterial).
- Since it is most often viral, treatment is largely supportive. Rest and activity limitation is important.
- Treatment of CHF may be necessary (i.e., diuretics, inotropic agents if severely ill). Gamma globulin also has been effective.

EXAM TIP

Risk Factors for Endocarditis:
- Previous endocarditis
- Dental procedures
- Gastrointestinal and genitourinary procedures
- IV drug use (usually affects the tricuspid valve)
- Indwelling central venous catheters
- Prior cardiac surgery.

WARD TIP

Always think of myocarditis when there is persistent tachycardia out of proportion to clinical setting (pain, dehydration, and fever can cause tachycardia, but should respond predictably to targeted therapy).

Pericarditis

ETIOLOGY

- Viral (most common).
- Bacterial infection (also common), *S. aureus, Haemophilus influenzae, Neisseria meningitidis*, streptococci, tuberculosis.
- Can occur with ARF.
- Complications from heart surgery.
- Collagen vascular diseases.
- Uremia.
- Medications (i.e., dantrolene, oncology agents).

PATHOPHYSIOLOGY

- Inflammation of the pericardium.
- Can progress to pericardial effusion or cardiac tamponade if significant fluid accumulates around the heart.

SIGNS AND SYMPTOMS

- Precordial pain with radiation to the shoulder and neck (often relieved by standing).
- **Pericardial friction rub** on auscultation.
- Signs of cardiac tamponade:
    - Distant heart sounds
    - Tachycardia
    - Pulsus paradoxus
    - Hepatomegaly and venous distention.

DIAGNOSIS

- CXR: A pear- or water bottle–shaped heart indicates a large effusion.
- Echocardiography is diagnostic (can also detect tamponade).

TREATMENT

- Treat the underlying disease process.
- Supportive treatment for viral etiologies, NSAIDS or steroids to decrease inflammation.
- Pericardiocentesis is indicated if effusion is present.
- Urgent drainage is indicated when symptoms of tamponade are present.

Congestive Heart Failure (CHF)

ETIOLOGY

- Caused from either congenital heart disease (CHD) or acquired heart disease.
- CHD: Most common cause is from volume or pressure overload.
- VSD, PDA, and endocardial cushion defects are the most common causes of CHF in the first 6 months of life.
- ASD can cause CHF in adulthood with cor pulmonale if unrepaired.

- Acquired heart disease: Potential causes of CHF are metabolic abnormalities (i.e., hypoxia, acidosis, hypoglycemia, hypocalcemia), myocarditis, rheumatic fever with carditis, cardiomyopathy, and drug toxicity.
  - Metabolic abnormalities (i.e., hypoxia, acidosis, hypoglycemia, hypocalcemia).
  - Myocarditis.
  - Rheumatic fever with carditis.
  - Cardiomyopathy.
  - Drug toxicity.

SIGNS AND SYMPTOMS

- Often similar symptoms to those found in respiratory illnesses: Tachycardia, tachypnea, shortness of breath, rales and rhonchi, intercostal retractions.
- Poor weight gain/poor feeding.
- Cold sweat on forehead.
- Older children develop peripheral edema.
- Gallop on auscultation.
- Hepatomegaly, jugular venous distention (JVD).

DIAGNOSIS

- CXR: Cardiomegaly, evidence of pulmonary edema.
- Echo: Enlarged ventricular chamber, impaired ventricular function.

TREATMENT

- Treat the underlying cause (i.e., surgical correction of CHD, correction of metabolic defects).
- Oxygen can be used if patient is hypoxic or in respiratory distress.
- Medication:
  - **Digitalis** is used to improve ventricular function. Contraindicated in complete heart block and hypertrophic cardiomyopathy.
  - **Diuretics** are used to ↓ volume overload and pulmonary edema. Most common are the "loop diuretics" (i.e., furosemide).
  - **Afterload-reducing agents** (i.e., angiotensin-converting enzyme [ACE] inhibitors, calcium channel blockers, nitroglycerin) are used to dilate peripheral vasculature and thus ↓ the work on the heart.

Vasculitides

HENOCH-SCHÖNLEIN PURPURA

- Immune-mediated vasculitis that affects the GI tract, joints, and kidneys and causes a characteristic rash (see Chapter 20).
- Palpable purpura.
- Most often occurs in winter months, following a group A streptococcal upper respiratory infection (URI).
- GI involvement is most significant, → vomiting and upper and lower GI bleeding. Gut wall hematomas can act as lead point for intussusception.
- Renal involvement, in the form of glomerulonephritis, with RBC casts, can progress to acute renal failure in 1–2% of cases. More common is chronic proteinuria, which can be a late sequela.
- Treatment is supportive, with full recovery within 4–6 weeks.

WARD TIP

A left-to-right shunt usually takes about 6 weeks to become significant enough to stress the left ventricle.

WARD TIP

Use of diuretics in CHF is preferred to salt and fluid restriction.

WARD TIP

Watch out for hypokalemia, as some diuretics, loop diuretics specifically, cause significant potassium loss.

WARD TIP

Hypokalemia can precipitate digitalis toxicity.

EXAM TIP

A 7-year-old boy presents with purpuric rash, swelling around both eyes and bloody bowel movements. He had a recent sore throat treated with penicillin. Think: Henoch-Schonlein Purpura.

WARD TIP

HSP can be diagnosed on the basis of clinical presentation (there is no confirmatory test other than characteristic histology on skin biopsy (usually not necessary or indicated). Complications to consider are intussusception in patients with acute, severe abdominal pain; prolonged renal involvement leading to renal insufficiency.

KAWASAKI DISEASE

A 2-year-old boy with fever for 7 days, often reaching 104°F (40°C), develops nonexudative conjunctival injection bilaterally; intensely erythematous lips, palms, and soles; generalized erythema multiforme; and an enlarged, tender anterior cervical lymph node. Blood cultures are sterile, and platelets are ↑. *Think: Kawasaki disease.*

Beware of his risk for coronary aneurysms and MI. Fever lasting for 5 or more days is the hallmark that must be present with at least four of the following features: Conjunctival injection, oropharyngeal mucous membrane changes, extremity swelling, polymorphous rash, and cervical lymphadenopathy.

DEFINITION

- Also known as mucocutaneous lymph node syndrome.
- Most common **acquired** heart disease in children.

ETIOLOGY

Acute vasculitis of mostly medium-sized arteries of unknown etiology.

EPIDEMIOLOGY

- Affects infants and young children (>80% under age 4 years).
- More common in Asians than other racial groups.
- More common in males than females (ratio 1.5:1).
- Most common in winter/spring months.

SIGNS AND SYMPTOMS

There is no confirmatory test for Kawasaki disease, but these tests are helpful in building a case to confirm clinical suspicion.
- Sterile pyuria.
- Aseptic meningitis.
- Thrombocytosis (usually after 7+ days of fever).
- Desquamation of fingers and toes.
- Elevated ESR or CRP.
- Elevated transaminases.
- Most significant sequelae:
    - Coronary aneurysms (usually resolve within 12 months of adequate therapy).
    - Pericardial effusion.
    - CHF.

DIAGNOSIS

- Diagnostic criteria: Fever for >5 days plus ≥4 of the following:
  1. Bilateral conjunctivitis (without exudate).
  2. Mucocutaneous lesions ("strawberry" tongue; dry, red, cracked lips; diffuse erythema of oral cavity).
  3. Changes in upper and lower extremities (erythema and/or edema of hands/feet).
  4. Polymorphic rash (usually truncal).
  5. Cervical lymphadenopathy (>1.5 cm in diameter), usually unilateral.
- Echocardiogram: Initial study at diagnosis to establish baseline and to evaluate for early coronary aneurysms; follow-up echo to establish presence or absence.

TREATMENT

- Used to prevent cardiac sequelae, the actual vasculitis self-resolves.
- Intravenous immune globulin (IVIG): Usually one dose of IVIG, 2 g/kg over 10–12 hours. Reduces incidence of coronary artery dilation by >90% (from 20% incidence to <2%).
- High-dose aspirin (80–100 mg/kg/day divided in four doses) until 48–72 hours after defervescence.
- If no coronary artery abnormality at time of echo, low-dose aspirin (3–5 mg/kg/day as a single daily dose) for 6–8 weeks, or until platelet count and ESR are normal.
- If coronary artery abnormality, continue indefinitely in consultation with a pediatric cardiologist. Aspirin is reduced after the patient is afebrile for 48 hours.
- Use of steroids remains controversial and typically reserved for cases refractory to repeat doses of IVIG.

> **EXAM TIP**
>
> Reye syndrome is associated with aspirin therapy during an infection with any viral etiology, commonly influenza or varicella. It presents as a progressive encephalopathy with liver dysfunction. Therefore, the use of ASA in children for Kawasaki disease is unique.

POLYARTERITIS NODOSA

DEFINITION

- A necrotizing inflammation of the small- and medium-sized muscular arteries.
- Involves renal and visceral vessels, spares pulmonary circulation.

SIGNS AND SYMPTOMS

- Prolonged fever, weight loss, malaise, subcutaneous nodules on extremities.
- Various rashes can be associated with this condition: Livedo reticularis.
- Often waxes and wanes.
- Gangrene of distal extremities is found in severe disease, caused by deep skin infarctions.

> **WARD TIP**
>
> Hypertension and abdominal pain can be important clues in polyarteritis nodosa.

DIAGNOSIS

- No diagnostic tests.
- Associated with abnormal cell counts (thrombocytosis, leukocytosis), abnormal urine analysis (proteinuria, hematuria, red cell casts), elevated acute-phase reactants, perinuclear anti-neutrophil cytoplasmic antibody (p-ANCA).
- Conclusive with findings of medium-sized artery aneurysms.
- Echocardiographic evidence of coronary artery aneurysms is diagnostic if other clinical evidence is present.

> **WARD TIP**
>
> Infantile polyarteritis nodosa occurs before the age of 2 years and most commonly causes coronary artery aneurysms—diagnosis is made postmortem because it clinically mimics Kawasaki disease.

TREATMENT

- Corticosteroids suppress the clinical manifestations.
- Cyclophosphamide or azathioprine may be required to induce remission.

TAKAYASU'S ARTERITIS

DEFINITION

- Also known as aortoarteritis, it is a large vessel vasculitis of unknown cause.
- Chronic inflammatory disease involving:
    - Aorta.
    - Arterial branches from the aorta.
    - Pulmonary vasculature.

> **EXAM TIP**
>
> Takayasu arteritis is also known as "pulseless disease" because peripheral artery pulses can be absent, decreased, or unequal.

PATHOPHYSIOLOGY

- Lesions are segmental and often obliterative.
- Aneurysmal and saccular dilation also occur.
- Thoracoabdominal aorta is the predominantly affected site in the pediatric population.

EPIDEMIOLOGY

Most patients are female, aged 4–45 years.

SIGNS AND SYMPTOMS

- A significant number of patients experience LV dysfunction and CHF (even in the absence of coronary artery involvement, HTN, or valvular abnormalities).
- A lymphocytic infiltration consistent with myocarditis is present in about 50% of patients.
- Other symptoms include fever, polyarthralgias, polyarthritis, and loss of radial pulsations.

TREATMENT

Corticosteroids may induce remission.

> **EXAM TIP**
>
> Essentially, Takayasu arteritis is giant cell arteritis of the aorta (and large branches).

> **EXAM TIP**
>
> In central cyanosis, there is systemic arterial desaturation. In peripheral cyanosis, systemic arterial oxygenation is normal, but there is increased oxygen extraction by the tissues.

> **EXAM TIP**
>
> Cyanotic Heart Defects
> Five T's and a P:
> **T**runcus arteriosus
> **T**ransposition of the great vessels
> **T**ricuspid atresia
> **T**etralogy of Fallot
> **T**otal anomalous pulmonary venous return (obstructive)
> **P**ulmonic atresia.

Cyanotic Heart Defects

CENTRAL CYANOSIS VS. ACROCYANOSIS

Central cyanosis:
- Involves mucous membrane, often evident as blue-tinged lips.
- Always pathologic in a newborn.
- Cyanosis in neonates is almost always due to either pulmonary or cardiac disease.
- >5 mg/dL of deoxyhemoglobin.

Acrocyanosis:
- Involves distal extremities.
- Normal in newborns.
- Peripheral cyanosis is the result of acrocyanosis, exposure to cold, and ↓ peripheral perfusion.

Children with Cyanotic Heart Disease are at ↑ Risk for Strokes and Scoliosis

TETRALOGY OF FALLOT (TOF)

The most common form of cyanotic CHD in the postinfancy period.

DEFINITION

Four anomalies constitute the tetralogy:

1. Right ventricular outflow tract obstruction (RVOTO).
2. VSD.
3. Overriding aorta.
4. RVH.

ETIOLOGY

Prenatal factors associated include maternal rubella or viral illness.

PATHOPHYSIOLOGY

The severity of the RVOT obstruction dictates the degree of shunting:

- **Minimal obstruction:** Pulmonary blood flow will increase as the PVR decreases, eventually causing CHF.
- **Mild obstruction:** Hemodynamic balance pressure between right and left ventricles is equal, thus no net shunting ("pink tet").
- **Severe obstruction: Blood cannot exit through the RVOT, pulmonary blood flow decreases → cyanosis.**

EPIDEMIOLOGY

Most common cyanotic heart defect in children who survive infancy.

SIGNS AND SYMPTOMS

- Failure to thrive (FTT) (if diagnosed late).
- "Conotruncal facies."
- Variable cyanosis (clubbing later if unrepaired).
- RV impulse; single S2, systolic ejection murmur at the upper left sternal border with or without ejection click.
- Squatting is a common posture in older children with uncorrected TOF.
    - Often occurs after exercise.
    - Desaturated blood is trapped in the lower extremities and systemic vascular resistance is increased, but the RVOT remains fixed. Therefore, squatting causes a decrease in the R → L shunt, increased pulmonary blood flow, and so increased arterial saturation.

"TET SPELLS"

- Most common: 2–6 months of age.
- Occur in the morning or after a nap when SVR is low.
- Precipitating factors:
    - Stress.
    - Drugs that ↓ SVR.
    - Hot baths.
    - Fever.
    - Exercise.
- Mechanism: Unknown, but likely due to ↑ cardiac output with fixed RVOT, → ↑ right-to-left shunting, which ↑ cyanosis.
- If prolonged or severe: Syncope, seizures, cardiac arrest.

DIAGNOSIS

- CXR (Figure 13-2).
- "Boot-shaped heart."
- ↓ pulmonary vascular markings.
- Right aortic arch (25%).

TREATMENT

- Patient's clinical status may prevent definitive repair initially.
- Shunting (i.e., Blalock-Taussig shunt) is often used when pulmonary stenosis is severe and an alternative route for blood to reach the lungs is necessary.
- Complete repair entails:
    - VSD closure.
    - Relief of RVOTO.
    - Ligation of shunts.
    - ASD/patent foramen ovale (PFO) closure.

WARD TIP

Key features of TOF:
- **VSD** (typically large enough to equalize pressures in right and left ventricles).
- **RVOTO** (e.g., pulmonary stenosis).
- **Aortic override** is variable.
- **RVH** is secondary to the RVOTO.

WARD TIP

Conotruncal facies is also described in DiGeorge syndrome. Children have hypertelorism, lateral displacement of the inner canthi, a flat nasal bridge, narrow palpebral fissues, and ear anomalies.

WARD TIP

During a "Tet spell" (a paroxysmal cyanotic event) the object is to increase SVR or reduce pulmonary hypertension in order to reduce the right to left shunting. Strategies include lifting legs to chest, squatting, giving oxygen or giving morphine (which reduces infundibular spasm resulting in increased pulmonary blood flow).

WARD TIP

CXR with the boot shape, ↓ pulmonary vascular markings, and a right aortic arch. *Think: Tetralogy of Fallot.*

WARD TIP

The Blalock-Taussig shunt increases pulmonary blood flow by grafting the subclavian or carotid artery to the pulmonary artery.

EXAM TIP

Without repair of TOF, mortality is:
- 50% by 3 years
- 90% by 20 years
- 95% by 30 years

(A) **(B)**
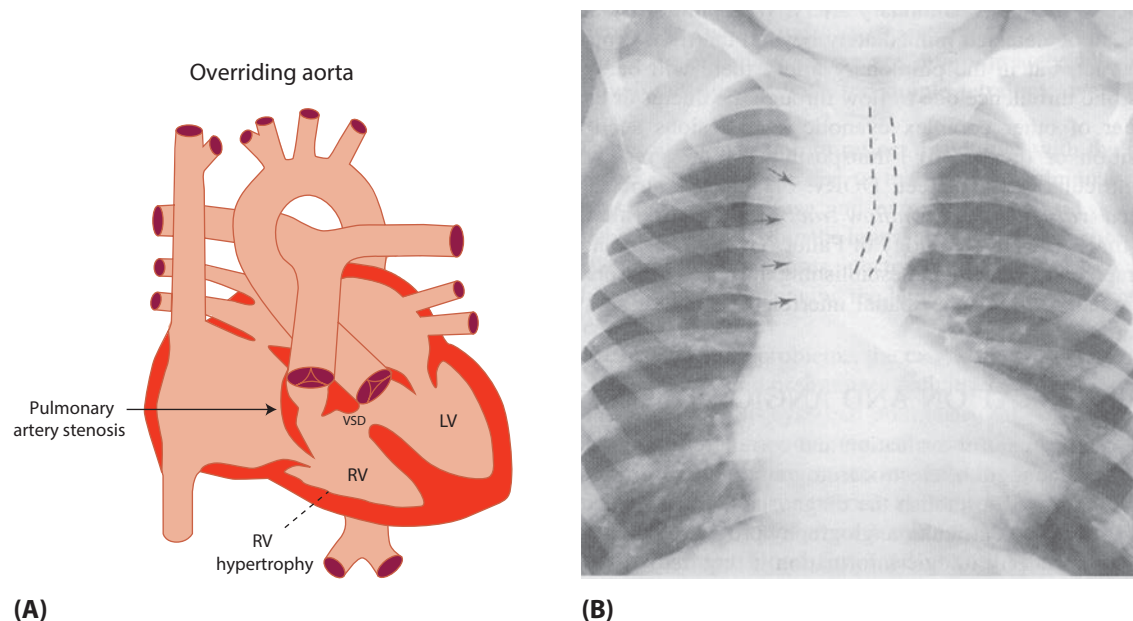
F I G U R E 1 3 - 2 . **Chest x-ray in tetralogy of Fallot.** Arrows indicate right-sided aortic arch and upper thoracic aorta. Dashed lines indicate right-sided aortic indentation on the air bronchogram. (X-ray reproduced, with permission, from Rudolph CD, et al (eds). *Rudolph's Pediatrics*, 21st ed. New York: McGraw-Hill, 2002: 1821.)

(A) **(B)**
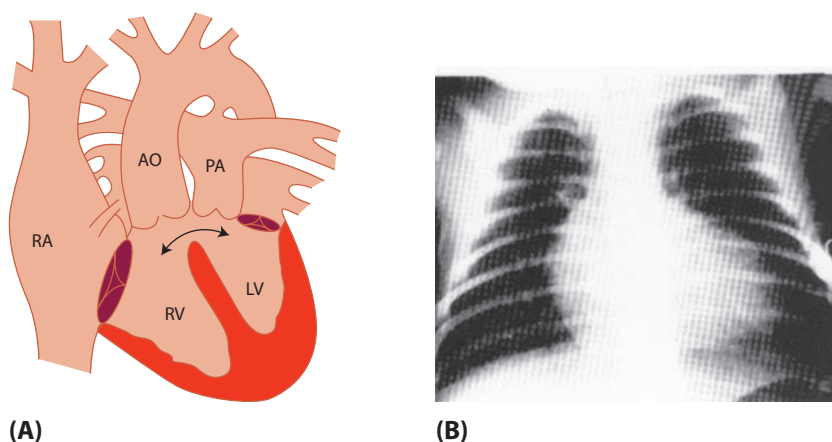
F I G U R E 1 3 - 3 . **Transposition of the great vessels.** "Egg on a string"—spinal column serving as the string and the globular presentation of the heart as the egg. (X-ray reproduced, with permission, from Moller JH, Neal WA. *Fetal, Neonatal, and Infant Cardiac Disease*, 2nd ed. Appleton & Lange, 1992: 532.)

TRANSPOSITION OF THE GREAT VESSELS

The most common cyanotic heart lesion in the newborn period.

PATHOPHYSIOLOGY

This lesion occurs when, in the development of the heart, the primitive heart loops to the left instead of the right and the following result (see Figure 13-3):
- Aorta originates from the RV.
- Pulmonary artery originates from LV.
- **A**orta is **a**nterior; **p**ulmonary trunk is **p**osterior.
- Right and left hearts are in parallel:
    - Pulmonary venous return goes to the pulmonary artery via left ventricle.
    - Systemic venous return goes to the aorta via the right ventricle.

- The presence of a VSD, ASD, or PDA is essential to survival—there MUST be a mixing lesion.
- A PDA alone is usually not sufficient to allow adequate mixing in the extrauterine environment.
- Cyanosis becomes more prevalent with the closure of the PDA.
- Presentation: CHF in the first week of life.
- CXR: Egg-shaped heart with a narrow mediastinum. Cardiomegaly with ↑ pulmonary vascular marking.

EPIDEMIOLOGY

Most common cyanotic congenital heart defect presenting in the neonatal period.

Intact Ventricular Septum (with no valve abnormality)	**With VSD (a large VSD allows adequate mixing)**

SIGNS AND SYMPTOMS

- Early cyanosis, a single S2, and no murmur.
- An intact atrial septum or very restrictive PFO is a medical emergency.

- Symptoms are related to ↑ pulmonary blood flow, with CHF sometimes occurring early.
- May have little cyanosis.

DIAGNOSIS

- ECG will be normal initially, but will demonstrate right ventricular hypertrophy by 1 month.
- CXR: "Egg on a string."

- ECG: Right or biventricular hypertrophy.

TREATMENT

- Patient is "ductal dependent" and will require prostaglandin E_1 (PGE_1) to keep the PDA patent.
- Early **balloon atrial septostomy** (BAS) is necessary to allow mixing of oxygenated and deoxygenated blood.
- Arterial switch procedure is definitive.

- PA band to control ↑ pulmonary blood flow.
- Arterial switch with VSD closure is definitive.

> **WARD TIP**
>
> Transposition of the great vessel: "Big blue baby" as intrauterine growth is normal. Does not have a murmur on exam.

> **WARD TIP**
>
> In the arterial switch operation, the key element is moving the origin of the coronary artery from the pulmonary artery to its rightful position on the aorta. This is source of greatest potential for complications.

TRUNCUS ARTERIOSUS

DEFINITION

- A persistent truncus is a single arterial trunk that emerges from the ventricles, supplying the coronary, pulmonary, and systemic circulations (see Figure 13-4).
- Association: DiGeorge syndrome.

TYPES

- **I:** Short common pulmonary trunk arising from right side of common trunk, just above truncal valve.
- **II:** Pulmonary arteries (PAs) arise directly from ascending aorta, from posterior surface.
- **III:** Similar to type II, with PAs arising more laterally and more distant from semilunar valves.
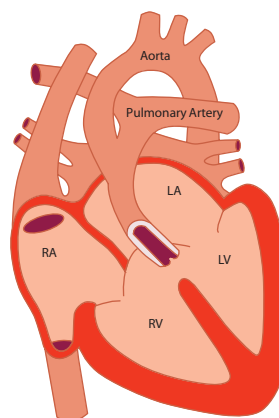
F I G U R E   1 3 - 4 .   Truncus arteriosus.

PATHOPHYSIOLOGY

- The valve has two, three, or four leaflets and is usually poorly functioning.
- The truncus overrides a VSD.

SIGNS AND SYMPTOMS

- Presentation: CHF and cyanosis in first week.
- Initial left-to-right shunt symptoms:
    - Dyspnea.
    - Frequent respiratory infections.
    - FTT.
- If pulmonary vascular resistance ↑, cyanosis ↑.
- Second heart sound is prominent and single due to the single semilunar valve.
- Peripheral pulses are strong, often bounding.
- Often, a systolic ejection click can be appreciated.

DIAGNOSIS

CXR shows cardiomegaly and ↑ pulmonary vascular markings.

TREATMENT

- Surgery must occur before patient develops significant pulmonary vascular disease (usually 3–4 months of age).
- VSD is surgically closed, leaving the valve on the LV side.
- The pulmonary arteries are freed from the truncus and are connected to a valved conduit (Rastelli procedure), which will serve as the new pulmonary trunk.

HYPOPLASTIC LEFT HEART SYNDROME (HLHS)

DEFINITION

The syndrome consists of the following (see Figure 13-5):
- Aortic valve hypoplasia, stenosis, or atresia with or without mitral valve stenosis or atresia.
- Hypoplasia of the ascending aorta.
- LV hypoplasia or agenesis.
- Mitral valve stenosis or atresia.
- The result is a single (right) ventricle that provides blood to the pulmonary system, the systemic circulation via the PDA, and coronary system via retrograde flow after crossing the PDA.
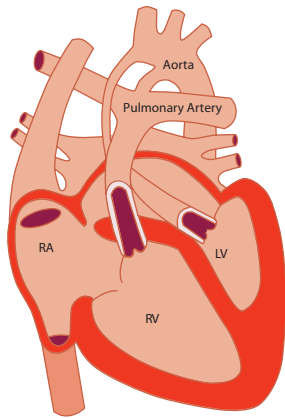
FIGURE 13-5. **Hypoplastic left heart syndrome.** Note small size of left ventricle.

- In utero:
  - All systemic blood flow is **ductus dependent**.
  - Pulmonary resistance > systemic vascular resistance.
  - Normal perfusion pressure is maintained with right-to-left shunt through PDA and pulmonary resistance.
- At birth:
  - PDA closes.
  - Systemic vascular resistance > pulmonary resistance.
  - PDA closure → ↓ cardiac output and ↓ systemic perfusion → metabolic acidosis.
  - PDA dependent until intervention is undertaken.

EPIDEMIOLOGY

The second most common congenital heart defect, presenting in the first week of life (and the most common cause of death from CHD in the first month).

SIGNS AND SYMPTOMS

- Pulses range from normal to absent (depending on ductal patency).
- Hyperdynamic RV impulse.
- Single S2 of ↑ intensity.
- Nonspecific systolic murmur at left sternal border (LSB).
- Skin may have a characteristic grayish pallor.

DIAGNOSIS

- CXR: Cardiomegaly with globular-shaped heart; ↑ pulmonary vascular markings, pulmonary edema.
- Echocardiogram is diagnostic, and this condition is typically detected in utero.

TREATMENT

- No intervention: Due to the high mortality and complicated surgical course of this disease, ethical dilemmas are frequent as to how far physicians should intervene.
- Three-stage surgery:
  - **Norwood procedure:** The pulmonary trunk is used to reconstruct the hypoplastic aorta, and the right ventricle subsequently becomes the functional left ventricle. This leaves the pulmonary arteries connected but separated from the heart. The pulmonary blood flow is then reestablished via systemic to pulmonary conduits from the subclavian arteries to the pulmonary arteries.

- **Glenn procedure:** The superior vena cava is connected to the right PA, restoring partial venous return to the lungs.
- **Fontan procedure:** The inferior vena cava is anastomosed to the PAs, resulting in complete venous diversion from the systemic circulation to the lungs.
- Heart transplant: This alternative occurs either as a primary intervention (if an organ is available) or after any of the previous palliative surgeries have provided maximal but ultimately insufficient benefit.

Acyanotic Heart Defects

Left-to-right shunt (see Figure 13-6).

SUBENDOCARDIAL CUSHION DEFECT

PATHOPHYSIOLOGY

Related to the ostium primum ASD, this defect results from abnormal development of the AV canal (endocardial cushions) resulting in:
- A VSD.
- An ostium primum ASD.
- Clefts in the mitral and tricuspid valves.

EPIDEMIOLOGY

- Association: Down syndrome (30% of patients with this defect have trisomy 21).
- Also frequently found with asplenia and polysplenia syndromes.

SIGNS AND SYMPTOMS

- Often the result of the specific components of the accumulated defects:
  - Holosystolic murmur from the VSD, if restrictive.
  - Systolic murmur from mitral and tricuspid valve insufficiency.
- High risk of developing Eisenmenger syndrome.
- ECG: Superior QRS axis with RVH, right bundle branch block (RBBB), and LVH, along with a prolonged PR interval.

| Subendocardial cushion defect | Atrial septal defect | Ventricular septal defect | Patent ductus arteriosus |
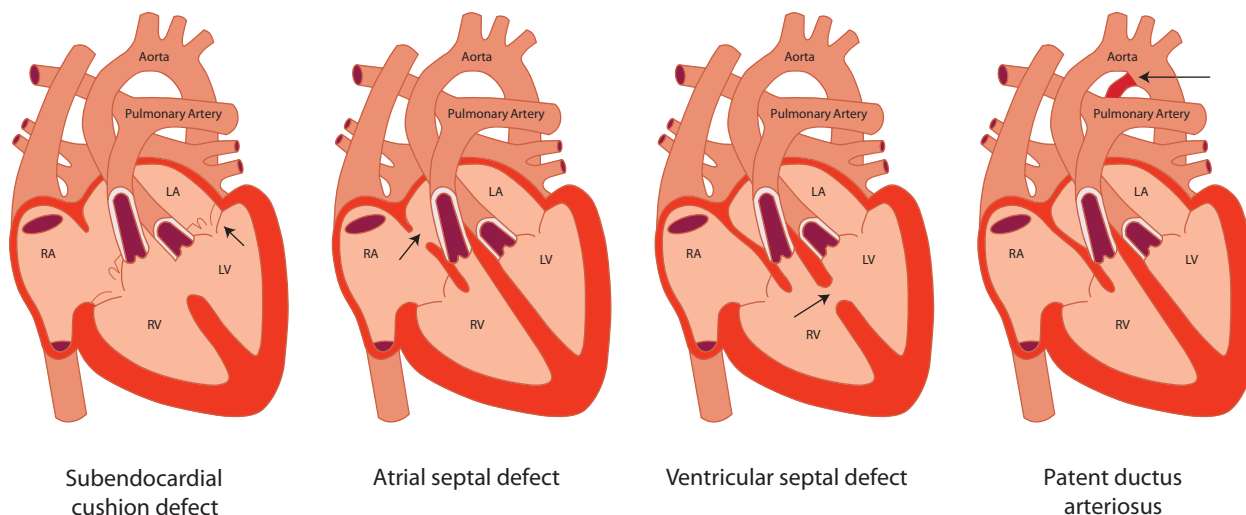
FIGURE 13-6.   Acyanotic heart defects.

TREATMENT

Surgical correction is sometimes the only option (despite high risk) when patient has an unbalanced AV canal.

ATRIAL SEPTAL DEFECT (ASD)

Ten percent of all congenital heart disease.

DEFINITION

Three types:
- **Secundum defect** (most common—50–70%): Located in the central portion of the atrial septum.
- **Primum defect** (about 30% of ASDs):
  - Located at the atrial lower margin.
  - Associated with abnormalities of the mitral and tricuspid valves.
- **Sinus venosus defect** (about 10% of ASDs): Located at the upper portion of the atrial septum and often extends into the superior vena cava.

EPIDEMIOLOGY

- A common "co-conspirator" in CHD.
- As many as 50% of patients with congenital heart defects have an ASD as one of the defects.
- More common in females (male-to-female ratio 1:2).

SIGNS AND SYMPTOMS

- Children with ASDs are typically asymptomatic.
- **Widely split and fixed S2**, because right-sided volume overload causes delayed closing of the pulmonic valve. Murmurs are uncommon, but may occur as patient gets older. Murmur is a secondary pulmonary flow murmur.
- Symptoms of CHF and pulmonary HTN occur in adults (second and third decades) due to persistent right side overload.

DIAGNOSIS

- ECG: The left-to-right shunt may produce right atrial enlargement and RVH.
- CXR: Cardiomegaly with ↑ pulmonary vascular markings.

TREATMENT

- Nearly 90% will close spontaneously.
- One hundred percent close if <3 mm.
- ASDs >8 mm are unlikely to close spontaneously.
- Surgical or catheter closure (via a "clamshell" or "umbrella" device) are used when indicated.

PATENT FORAMEN OVALE (PFO)

- The foramen ovale is used prenatally to provide oxygenated blood from the placenta to the left atrium.
- It normally functionally closes when ↑ left atrial pressure causes the septa to press against each other (many remain "probe-patent" into adulthood).
- In some children, the tissue of the foramen ovale is insufficient to cover the foramen (either from insufficient growth or becoming stretched from ↑ pressure or volume).
- Some CHDs require a PFO for patient survival after birth (e.g., tricuspid and mitral atresia, TAPVR).

WARD TIP

AV canal, AVSD, and endocardial cushion defect are equivalent terms.

EXAM TIP

ASD is the most common congenital heart lesion recognized in adults.

VENTRICULAR SEPTAL DEFECT (VSD)

A 2-month-old male born at term appeared well until 3 weeks ago, when he became dyspneic and had difficulty feeding. A loud pansystolic murmur is heard at the left lower sternal border, and ECG shows LVH and RVH. *Think: VSD.*

Small VSD causes no symptoms. Large VSD may result in left-to-right shunt and pulmonary HTN. Left-sided volume overload and RVH are suggestive of a large VSD.

EPIDEMIOLOGY

- The most common form of recognized congenital heart disease (30–60% of all patients with CHDs).
- Usually membranous, as opposed to in the muscular septum.
- Occurs in 2 per 1000 live births.

SIGNS AND SYMPTOMS

Dependent on defect size:
- Small VSDs:
  - Usually asymptomatic.
  - Normal growth and development.
  - High-pitched, holosystolic murmur (more turbulent flow).
  - No ECG or CXR changes.
- Large VSDs:
  - Can → CHF and pulmonary HTN.
  - May have FTT.
  - Lower-pitched murmur (less turbulent flow); intensity dependent on the degree of shunting.

DIAGNOSIS

- ECG: LVH.
- CXR: Cardiomegaly with ↑ pulmonary vascular markings.

TREATMENT

- Spontaneous closure:
  - Muscular defects are most likely to close (up to 50%), with closure occurring during the first year of life.
  - Inlet and infundibular defects do not reduce in size or close.
- Intervention is based on the development of CHF, pulmonary HTN, and growth failure.
- Initial management with diuretics and digitalis.
- Surgical closure is indicated when medical therapy fails.
- Catheter-induced closure devices are less commonly used with VSDs than ASDs.
- Endocarditis prophylaxis.

Patent Ductus Arteriosus (PDA)

PATHOPHYSIOLOGY

- Most often a problem in premature neonates:
  - Left-to-right shunts are handled poorly by premature infants.
  - Many develop idiopathic respiratory distress syndrome.
  - Some progress to develop left ventricular failure.

- Failure of spontaneous closure:
  - Premature infants: Due to ineffective response to oxygen tension.
  - Mature infants: Due to structural abnormality of ductal smooth muscle.

EPIDEMIOLOGY

- PDA is more common in females (male-to-female ratio 1:3).
- Incidence is higher at higher altitudes due to lower atmospheric oxygen tension.
- Maternal rubella in the first trimester has also been implicated in PDA.

SIGNS AND SYMPTOMS

- Small PDAs usually are asymptomatic.
- Large PDAs ↑ incidence of lower respiratory tract infections and CHF.
- Machinery-like murmur.
- Bounding peripheral pulses and wide pulse pressure.
- If Eisenmenger syndrome results, patient may have cyanosis restricted to the lower extremities as oxygen poor blood mixes into the aorta distal to the subclavian arteries.

TREATMENT

- Indomethacin: Used in premature infants. Inhibits prostaglandin synthesis, → closure.
- Catheter closure via devices such as double-umbrella devices and coils in older children.
- Surgical ligation and division via a left lateral thoracotomy.
- An occasional complication is recurrent laryngeal nerve injury → hoarseness.
- Eisenmenger syndrome is a contraindication to surgery.

PDA-Dependent Congenital Heart Abnormalities

- PDA-dependent congenital heart abnormalities include:
  - Tetralogy of Fallot.
  - Tricuspid atresia.
  - TAPVR with obstruction.
  - Aortic coarctation (severe).
  - Pulmonic atresia.
  - Hypoplastic left heart.
- Prostaglandin E_1 (PGE_1) can be potentially lifesaving in a cyanotic newborn with PDA-dependent congenital heart abnormalities.
- CHD presenting in first 2–3 weeks of life are usually due to ductal-dependent lesions.

DICATIONS FOR PGE₁ ADMINISTRATION

- Critically ill newborn with:
  - Suspected LV outflow tract obstruction.
- Dose:
  - 0.05 to 0.1 μg/kg/min (to reopen the ductus).
  - 0.01 μg/kg/min (to maintain ductal patency).
- Side effects:
  - **Apnea**: Endotracheal intubation prior to transport.
  - Fever, hypotension, and seizures.
- **Do not delay PGE₁ administration** in critically ill neonates with suspected ductal-dependent lesion pending definitive cardiac diagnosis.

EXAM TIP

- In the normal neonate, the ductus arteriosus closes primarily in response to a ductal $PO_2 > 50$ mm Hg.
- PDA closes within 15 hours after birth.
- Complete closure by 3 weeks to become the ligamentum arteriosum.
- Hypoxia and prematurity have a tendency to keep the ductus arteriosus patent.
- Can be a cause of apnea and bradycardia of prematurity.

WARD TIP

Subacute bacterial endocarditis (SBE) is more common in small PDAs than large ones.

EXAM TIP

Infective endocarditis is the most common complication of PDA in late childhood.

WARD TIP

Prostaglandins keep the PDA Patent. It is a critical life-saving intervention in the cyanotic, hypotensive infant.

EISENMENGER SYNDROME

- Can occur in unrepaired left-to-right shunts (i.e., VSD) that cause an ↑ pressure load on the pulmonary vasculature.
- Pressure overload on the pulmonary vasculature can result in irreversible changes in the arterioles.
- This develops into pulmonary vascular obstructive disease, usually over several years.
- The pulmonary HTN reduces the left-to-right shunt and previous LVH often resolves.
- Persistent HTN maintains an enlarged right ventricle and can dilate the main pulmonary segment (this becomes evident on CXR).
- Avoidance of this condition via surgical correction of CHD is essential, as it causes irreversible changes.

Congenital Valvular Defects

See Figure 13-7.

Tricuspic atresia   Pulmonary atresia   Aortic insufficiency

Mitral stenosis   Mitral valve prolapse
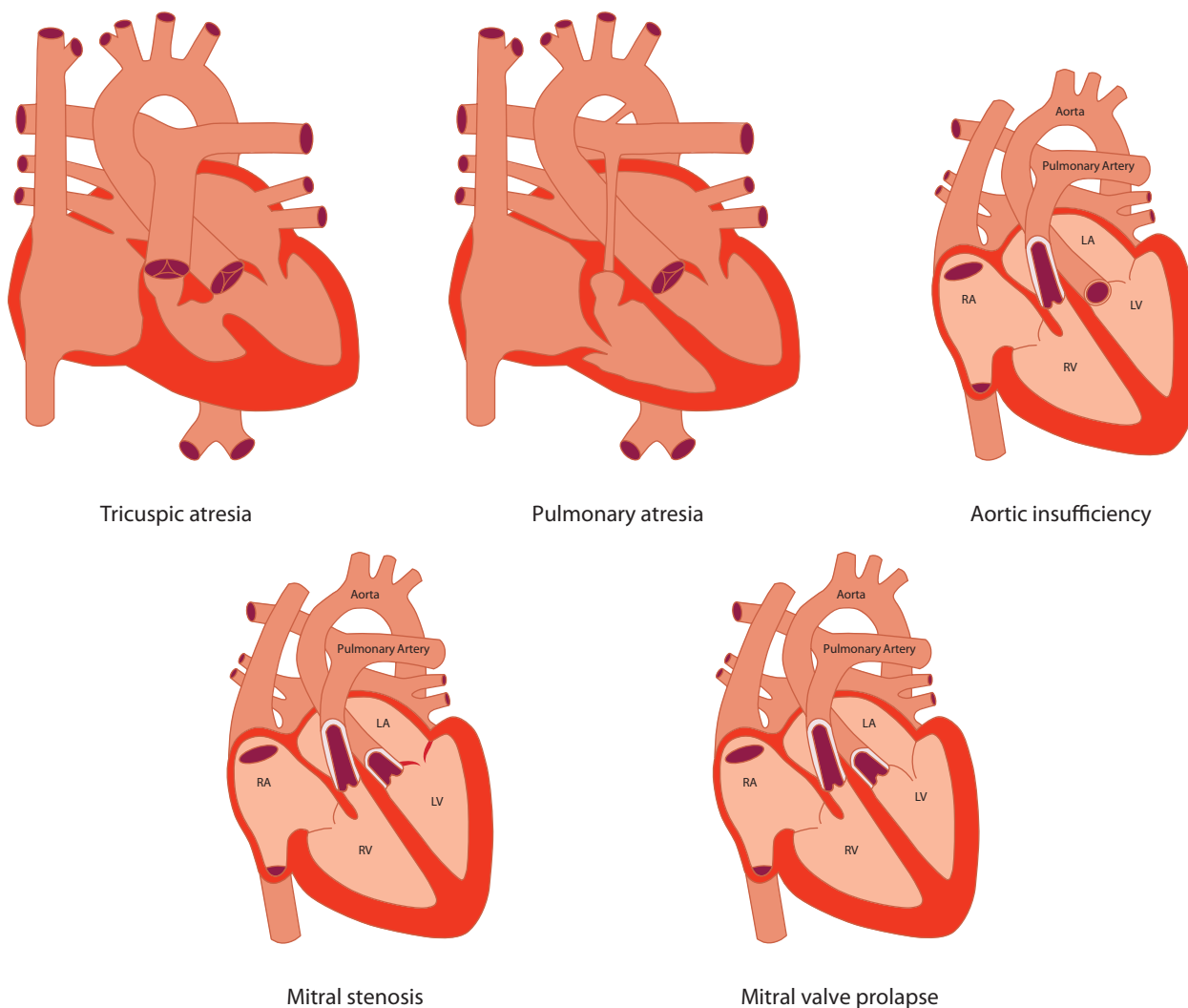
F I G U R E 1 3 - 7 .   **Congenital valvular defects.**

TRICUSPID ATRESIA

DEFINITION

RV inlet is absent or nearly absent:
- Eighty-nine percent have no evidence of tricuspid valve tissue, only dimple.
- Seven percent have a membranous septum forming part of the right atrial floor.
- Three percent are Ebstein's.
- One percent have a tiny, imperforate valvelike structure.

EPIDEMIOLOGY

- ASD and/or VSD is usually present.
- Seventy-five percent will present with cyanosis within the first week.

SIGNS AND SYMPTOMS

LV impulse displaced laterally.

DIAGNOSIS

ECG: LVH, prominent LV forces (due to ↓ RV voltages).

TREATMENT

- PGE_1 to maintain ductal patency.
- Surgical intervention.
- Modified Blalock-Taussig (BT) shunt.
- Glenn procedure, followed by Fontan procedure.

PULMONARY ATRESIA (WITH INTACT VENTRICULAR SEPTUM)

SIGNS AND SYMPTOMS

- Cyanosis within hours of birth (PDA closing).
- Hypotension, tachypnea, acidosis.
- Single S2, with a holosystolic murmur (tricuspid regurgitation).

DIAGNOSIS

- ECG: ↓ RV forces and occasionally RVH.
- CXR: Normal to enlarged RV with ↓ pulmonary vascular markings.

TREATMENT

- PGE_1 to maintain ductal patency.
- BAS (sometimes).
- Reconstruction of RVOT with transannular patch or pulmonary valvotomy.
- ASD left open to prevent systemic venous HTN.

AORTIC STENOSIS

> A 4-year-old boy with recurrent episodes of syncope while playing has a harsh systolic murmur radiating to the carotids, diminished cardiac pulses, and severe LVH. *Think: Congenital aortic stenosis.*
>
> Angina, syncope, and congestive heart failure are the presentation of aortic stenosis. Syncope during exertion occurs due to the reduced cerebral perfusion when arterial pressure declines. However, many patients now are diagnosed before the development of these symptoms on the basis of the finding of a systolic murmur followed by echocardiography.

Epidemiology

Eighty-five percent of congenitally stenotic aortic valves are bicuspid.

Signs and Symptoms

- Severe stenosis generally presents shortly after birth.
- Older children may complain of chest or stomach pain (epigastric).
- Patients with untreated severe aortic stenosis are at risk for syncope and sudden death.
- The characteristic murmur is a **crescendo-decrescendo systolic murmur.**
- A **systolic ejection click** is also common (particularly if bicuspid aortic valve).
- In severe disease, paradoxical splitting of S2 occurs (split narrows with inspiration).

Diagnosis

- Clinical findings, including ECG findings, and symptoms can be deceiving.
- Echo or catheterization to evaluate pressure differences between the aorta and left ventricle is essential.

Treatment

- Surgical or interventional balloon.
- Valvotomy is most common intervention:
    - Indication is usually if the measured catheterization gradient is >50 mm Hg.
    - High incidence of recurrent stenosis.
- Valve replacement: Deferred, when possible, until patient completes growth.

> **EXAM TIP**
>
> Supravalvular aortic stenosis is associated with idiopathic hypercalcemia and with Williams syndrome.

AORTIC INSUFFICIENCY

Epidemiology

Uncommon and usually associated with mitral valve disease or aortic stenosis as in the case of Rheumatic heart disease.

Signs and Symptoms

- A diastolic, decrescendo murmur is present at the left upper sternal border.
- Presentation with symptoms indicates advanced disease.
- Chest pain and CHF are ominous signs.

Diagnosis

CXR: LV enlargement, dilated ascending aorta.

Treatment

- Surgery or balloon valvuloplasty to treat aortic stenosis may worsen the insufficiency.
- Aortic valve replacement is the only definitive therapy.

> **WARD TIP**
>
> People with Marfan syndrome frequently have aortic insufficiency as well.

MITRAL STENOSIS

> CASE: A 16-year-old girl comes in for a well-child visit. She complains of some shortness of breath. The girl was adopted from the Ukraine as a child, and her vaccination status is unknown. She has a diastolic murmur on exam. Think: mitral stenosis.
>
> Mitral stenosis is usually a sequela of untreated rheumatic fever, rarely seen in the United States. Also recall, diastolic murmurs are ALWAYS pathologic.

EPIDEMIOLOGY

- Rare in children; usually a sequela of ARF.
- Congenital forms are generally severe.

SIGNS AND SYMPTOMS

- When symptomatic, dyspnea is the most common symptom.
- Weak peripheral pulses with narrow pulse pressure.
- An **opening snap** is heard on auscultation as atrial pressures snap open the stiff, calcified valve; also, a **presystolic (late diastolic) murmur** may be heard.
- Pulmonary venous congestion occurs, →:
  - CXR evidence of interstitial edema.
  - Hemoptysis from small bronchial vessel rupture.

TREATMENT

- Balloon valvuloplasty.
- Surgical:
  - Commissurotomy.
  - Valve replacement.

MITRAL VALVE PROLAPSE

PATHOPHYSIOLOGY

Caused by thick and redundant valve leaflets that bulge into the mitral annulus.

EPIDEMIOLOGY

- Usually occurs in older children and adolescents.
- Has a familial component (autosomal dominant).
- Nearly all patients with Marfan syndrome have it.

SIGNS AND SYMPTOMS

- Auscultation: Midsystolic click and late systolic murmur.
- Often asymptomatic with some history of palpitations and chest pain.

TREATMENT

Management is symptomatic (e.g., β blocker for chest pain).

Other Congenital Cardiovascular Defects

COARCTATION OF THE AORTA

PATHOPHYSIOLOGY

- Most commonly found in the juxtaductal position (where the ductus arteriosus joins the aorta).
- Development of symptoms may correspond to the closure of the ductus arteriosus (the patent ductus provides additional room for blood to reach the postductal aorta).

EPIDEMIOLOGY

- More common in males than females (male-to-female ratio 2:1).
- Association: Seen in one-third of patients with Turner syndrome.

SIGNS AND SYMPTOMS

Clinical Presentation of Symptomatic Infants
- FTT, respiratory distress, and CHF develop in the first 2–3 months of life.
- Lower extremity changes: ↓ pulses in the lower extremities.

WARD TIP

Differentiate opening SNAP (mitral stenosis) and mid-systolic CLICK (mitral prolapse).

WARD TIP

Coarctation of the aorta is associated with Turner syndrome.

WARD TIP

The presence of ↓ pulses in the lower extremities is the clue for diagnosis of coarctation.

WARD TIP

Comparison of the right upper extremity blood pressures and pulse oximeter readings with the lower extremity should be performed with a possible diagnosis of coarctation.
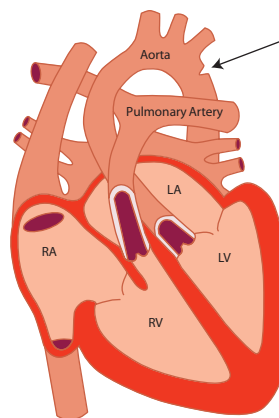
FIGURE 13-8. Coarctation of the aorta.

- Acidosis may develop as the lower body receives insufficient blood.
- Usually, a murmur is heard over the left back.

Clinical Presentation of Asymptomatic Infants or Children
- Normal growth and development.
- Occasional complaint of leg weakness or pain after exertion.
- ↓ pulses in the lower extremities.
- Upper-extremity HTN (or at least greater than in the lower extremities).

DIAGNOSIS

CXR: "3 sign," dilated ascending aorta that displaces the superior vena cava to the right (see Figure 13-8).

TREATMENT

- Resection of the coarctation segment with end-to-end anastomosis is the intervention of choice for initial treatment.
- Allograft patch augmentation can also be used.
- Catheter balloon dilation can be used:
    - Has a higher restenosis rate than surgery.
    - Has an ↑ risk of producing aortic aneurysms.
    - Balloon dilation is more frequently used when stenosis occurs at the surgical site of a primary reanastamosis.

EBSTEIN'S ANOMALY

DEFINITION

Components of the defect (see Figure 13-9):
- The tricuspid valve is displaced apically in the right ventricle.
- The valve leaflets are redundant and plastered against the ventricular wall, often causing functional tricuspid atresia.
- The right atrium is frequently the largest structure.

EPIDEMIOLOGY

Without intervention:
- CHF in first 6 months.
- Nearly 50% mortality.

SIGNS AND SYMPTOMS

- Growth and development can be normal depending on severity of the lesion.
- Older patients usually complain of dyspnea, cyanosis, and palpitations.
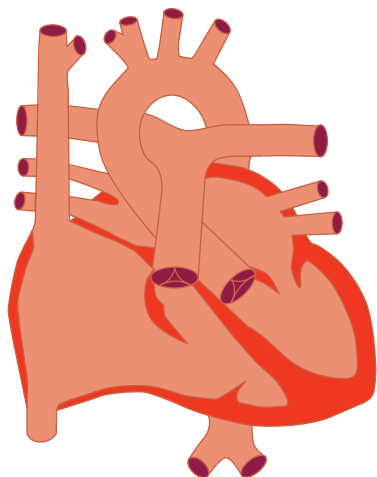
FIGURE 13-9.   Ebstein's anomaly.

- Widely split S1, fixed split S2, variable S3, and S4 (characteristic triple or quadruple rhythm).
- Holosystolic murmur at left lower sternal border.
- Opening snap.
- Cyanosis from atrial right-to-left shunt.

DIAGNOSIS

- ECG: Right-axis deviation, right atrial enlargement, RBBB. WPW is present in 20%, as a dilated right atrium predisposes to accessory pathway formation due to increased surface area.
- CXR: Cardiomegaly ("balloon-shaped") "wall-to-wall heart" in severely affected infants.
- "Enlarged heart" on CXR can be defined by the cardiothoracic ratio: the ratio of the largest diameter of the cardiac silhouette over the full thoracic diameter. A CT ratio of >0.6 is considered enlarged in children (as opposed to 0.5 in adults).
- Echocardiogram is diagnostic.

TREATMENT

Intervention (87% do well):
- Glenn procedure to ↑ pulmonary blood flow (passive venous blood flow to pulmonary artery).
- Severely affected infants may require aortopulmonary shunt.
- Tricuspid valve replacement or reconstruction.
- Right atrial reduction surgery.
- Ablation of accessory conduction pathways.

TOTAL ANOMALOUS PULMONARY VENOUS RETURN (TAPVR)

The pulmonary veins bring the blood from the lungs to the right atrium (instead of the left atrium).

PATHOPHYSIOLOGY

- See Figure 13-10A and B.
- No communication exists between the pulmonary veins and the left atrium.
- All pulmonary veins drain to a common vein.
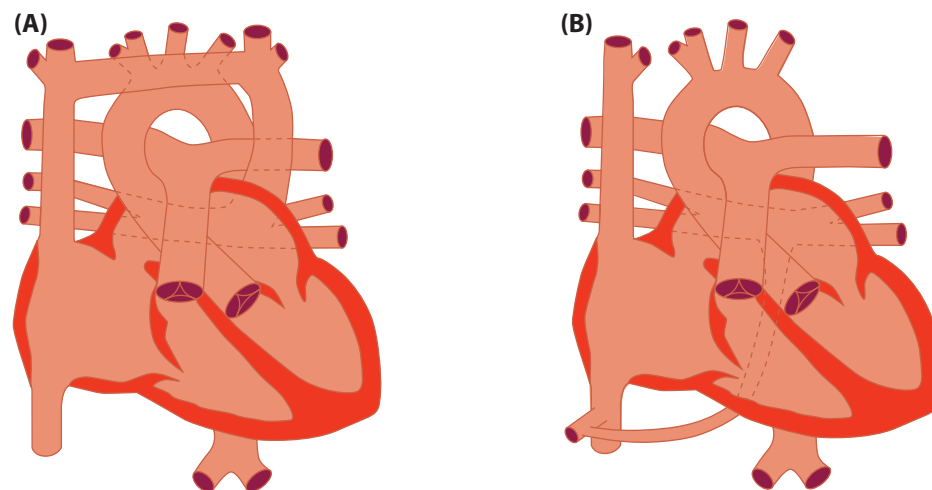
F I G U R E   1 3 - 1 0 .   **Total anomalous pulmonary venous return. (A)** Supracardiac view. **(B)** Infracardiac view.

- The common vein drains into the:
  - Right superior vena cava (50%).
  - Coronary sinus or right atrium (20%).
  - Portal vein or inferior vena cava (20%).
  - Combination of the above types (10%).
- An ASD is needed for survival.

Epidemiology

Dramatically more common in males (male-to-female ratio 4:1).

Signs and Symptoms/Diagnosis/Treatment

Presence or absence of obstruction of pulmonary venous return changes the clinical presentation.

TAPVR with Obstruction
- Obstruction defined as ↑ pulmonary artery pressure (and subsequent pulmonary edema) caused by pulmonary vascular resistance in response to excessive volume being pumped into the lungs from the RV.
- This leads to increased pulmonary pressures resulting in right ventricular and ultimately right atrial pressures. The effect of this is a right-to-left shunt and cyanosis.
- Presents with early, severe respiratory distress and cyanosis, no murmur, and hepatomegaly.
- CXR: Normal-size heart, pulmonary edema.
- Echocardiogram is diagnostic.
- Management: BAS or immediate corrective surgery.

TAPVR Without Obstruction
- Free communication between right atrium and left atrium.
- Large right-to-left shunt ("large ASD").
- Presents later during first year of life, with mild FTT, recurrent pulmonary infections, tachypnea, right heart failure, and rarely cyanosis.
- CXR: Cardiomegaly, large PAs; ↑ pulmonary vascular markings ("snowman" or "figure eight" sign) is found in infants >4 months old.
- Management: Surgical movement of pulmonary veins to the left atrium.

HYPERTROPHIC OBSTRUCTIVE CARDIOMYOPATHY

- Autosomal dominant 60%, sporadic 40%.
- Sudden death: **4% to 6% incidence.**
- Asymmetrical septal hypertrophy or idiopathic hypertrophic subaortic stenosis (IHSS) is the most common form.
- Systolic ejection murmur heard best with maneuvers that decrease preload (e.g., Valsalva, squatting). Decreased preload means decreased ventricular volume, which then allows the hypertrophic ventricular septum to come in closer proximity to the aortic outflow tract, causing increased turbulence and an audible murmur.
- Murmur decreases with increased preload, because the larger ventricular volume expands the outflow tract, causing less turbulent flow.
- ECG: LVH and left atrial enlargement, large Q wave (indicates septal hypertrophy).
- Echo: Asymmetrical septal hypertrophy, outflow obstruction (which predict the severity of disease).

TREATMENT

- Moderate restriction of physical activity.
- β blocker or calcium channel blocker to improve filling.
- Endocarditis prophylaxis.

NOTES

Renal, Gynecologic, and Urinary Disease

Acid-Base Disorders

NORMAL ACID-BASE BALANCE

- pH 7.4.
- P_{CO_2} 40.
- O_2 sat 98–100%.
- Bicarbonate 22–28.

DIAGNOSIS

- Diagnose acid-base disorders by obtaining an arterial blood gas (ABG—pH and P_{CO_2}) and an electrolyte panel (HCO_3^-).
- Assess the acid-base disorder step by step:
  - Is the primary disorder an acidosis (pH <7.36) or alkalosis (pH >7.44)?
  - Is the disorder respiratory (pH and P_{CO_2} move in opposite directions)?
  - Is the disorder metabolic (pH and P_{CO_2} move in the same direction)?
  - Has there been respiratory/metabolic compensation? Is it a simple or mixed disorder?

ACIDOSIS

- Acidemia refers to an arterial pH <7.36, caused by metabolic (decreased serum HCO_3^-) or respiratory (increased P_{CO_2}) acidosis.
- There is an extracellular shift of potassium (exchange hydrogen cation for potassium cation) and decreased binding of calcium to albumin, which may lead to hyperkalemia and hypercalcemia.
- There is a lower affinity between O_2 and Hb and more oxygen is released to tissues. This shifts the oxygen dissociation curve to the right.

METABOLIC ACIDOSIS

- Drop in pH due to a decreased serum HCO^{3-}.
- Decreased serum HCO_3^- may result from (1) increased production of acids, (2) decreased excretion of acids, or (3) loss of alkaline fluids.
- The anion gap (AG) helps identify the cause of metabolic acidosis. It reflects unmeasured serum ions (organic acids, phosphates, etc.).
  - $AG = [Na^+] - ([Cl^-] + [HCO_3^-])$.
  - In children, an AG above 14 is considered elevated.
- Normal AG metabolic acidosis (hyperchloremic metabolic acidosis) results when low serum HCO_3^- is balanced by increased renal Cl^- reabsorption. Etiologies include:
  - Diarrhea (most common), due to excessive gastrointestinal HCO_3^- loss.
  - Renal tubular acidosis, caused by ineffective reabsorption of HCO_3^- proximally (type 2) or ineffective excretion of H+ distally (type 1).
- AG metabolic acidosis can be caused by exogenous sources (drugs), endogenous production of acid (lactic acidosis, ketoacidosis, etc.), or retention of acid due to renal failure (uremia). See MUDPILES.
- Respiratory compensation (tachypnea) begins within 30 minutes. Severe metabolic acidosis (pH <7.2) results in compensatory hyperventilation (Kussmaul's breathing).
  - Appropriate change in P_{CO_2} can be predicted with the Winter's formula (Expected $P_{CO_2} = (1.5 \times$ serum $HCO_3^-) + 8 \pm 2$).
- Treat by correcting the underlying disorder. Oral bicarbonate may be used for chronic metabolic acidosis. For acute metabolic acidosis, use IV bicarbonate only in severe cases (pH <7.1).

WARD TIP

The notation commonly used for blood gases whether arterial or venous is: pH/P_{CO_2}/PO_2/calculated HCO_3^-/calculated Sa_{O_2}.

WARD TIP

Normal ABG values = 7.36–7.44/36–44/80–100/21–27

WARD TIP

ABGs show a calculated value of bicarbonate. Electrolyte panels show a measured value of bicarbonate (venous CO_2) and are therefore more reliable.

WARD TIP

Causes of anion gap metabolic acidosis:
MUDPILES
Methanol
Uremia
Diabetic ketoacidosis (DKA)
Propylene glycol/Paraldehyde
Isoniazid
Lactate
Ethylene glycol
Salicylates

RESPIRATORY ACIDOSIS

- Drop in pH due to pulmonary retention of CO_2 ($Paco_2$ >40 mm Hg).
- May be acute or chronic. Causes include respiratory suppression due to loss of CNS control, muscular dysfunction, acute lung injury, chronic lung disease, chest wall restriction, etc.
- Renal compensation consists of increased excretion of H^+ and reabsorption of HCO_3^-.
- Children with acute respiratory acidosis due to hypoventilation require close monitoring and may need ventilator support in severe cases. Correct electrolyte abnormalities, ensure adequate O_2, and correct reversible causes.

ALKALOSIS

- Alkalemia refers to an arterial pH >7.44, caused by metabolic (increased HCO_3^-) or respiratory (decreased Pco_2) alkalosis.
- May induce hypokalemia (intracellular shift of potassium for hydrogen cations) and hypocalcemia.
- Decreased affinity between O_2 and Hb and decreased oxygen delivery.

METABOLIC ALKALOSIS

> A 6-week-old child has a 2-day history of projectile vomiting that is not bile-stained. He is dehydrated and slightly jaundiced. *Think: Pyloric stenosis.*
> The classic symptom of pyloric stenosis is nonbilious, projectile vomiting. Progressive vomiting results in hypochloremic hypokalemic metabolic alkalosis from loss of gastric HCl. Classic but infrequent physical exam finding is olive-shaped mass in right upper quadrant. Treatment includes IV fluids to normalize acid-base status and correct electrolyte abnormalities and surgical consult for myomectomy.

- Increase in pH due to increased serum HCO_3^-.
- In children, metabolic alkalosis is most commonly caused by gastric (acidic) fluid loss (vomiting). Other causes include volume contraction due to diuretics, cystic fibrosis, primary hyperaldosteronism, Bartter syndrome, Liddle syndrome, and milk-alkali syndrome.
    - Urinalysis (UA) is the best initial step in evaluation to determine if the extracellular fluid (ECF) volume is contracted or expanded.
- Respiratory compensation is expected to cause 0.7 mm Hg increase in $Paco_2$ for every 1 mEq/L increase in serum HCO_3^-.
- Treatment includes volume repletion in cases of ECF contraction, correction of electrolyte abnormalities, potassium-sparing diuretics or acetazolamide for patients with high-volume states, dialysis in renal failure patients, and reversal of the underlying cause.

RESPIRATORY ALKALOSIS

- Increase in serum pH due to **hyperventilation**, leading to loss of CO_2 ($Paco_2$<40 mm Hg).
- Causes include anxiety, asthma, pulmonary embolism, and pneumonia.
- Renal compensation occurs via excretion of HCO_3^-.
- Correct the underlying disorder. Breathing into a paper bag can be useful for psychogenic hyperventilation.

WARD TIP

Expected Pco_2 in metabolic acidosis should be calculated with Winter's formula and compared with measured Pco_2 to see if compensation is appropriate.

$$Expected\ Pco_2 = 1.5\ (measured\ HCO_3^-) + 8 \pm 2$$

Failure of compensation is indicative of a mixed acid-base disorder.

WARD TIP

Vomiting causes dehydration with what acid base disorder? Metabolic alkalosis and low urine chloride (you vomit up HCl, causing loss of acid and chloride!).

WARD TIP

Hypokalemia is a common electrolyte abnormality seen in metabolic alkalosis. Treat with KCl.

WARD TIP

In metabolic disorders, respiratory compensation occurs immediately. In respiratory disorders, metabolic compensation takes longer to occur.

EXAM TIP

What do you do with an asthmatic in respiratory distress who has a normal pH and normal Pco_2? Get ready for intubation — they are tiring out. An asthmatic in only mild distress is expected to have respiratory alkalosis from tachypnea.

MIXED ACID-BASE DISORDER

- Simultaneous presence of more than one acid-base disorder.
- Suspect mixed acid-base disorder when the compensation is less than or greater than expected.
- Suspect mixed acid-base disorder if the pH corrects completely to normal.

Renal Tubular Acidosis (RTA)

A 1-year-old child is brought into the ED with vomiting, constipation, and decreased urine production. The child is found to have normal anion gap metabolic acidosis. A renal ultrasound reveals nephrocalcinosis. *Think: Renal tubular acidosis.*

Renal tubular acidosis is characterized by normal anion gap metabolic acidosis. A urine pH <5.5 suggests proximal RTA, whereas urine pH >5.5 suggests distal RTA. Presence of nephrocalcinosis and hypercalciuria is also suggestive of distal RTA.

DEFINITION

- A disorder of the renal tubules with preservation of glomerular function.
- Normal anion gap (hyperchloremic) metabolic acidosis is due to impaired urinary acidification (retention of H^+ or loss of bicarbonate).
- The three common types are types 1,2, and 4. Type 3 RTA is exceedingly rare. Type 1 is the most common form.

TYPE 1—DISTAL RTA

PATHOPHYSIOLOGY

- Hyperchloremic metabolic acidosis with a high urinary pH (>5.5) due to impaired acid secretion by the distal tubule and collecting duct.
- Compensatory excretion of other cations causes hypokalemia and elevated calcium in urine.
- Serum bicarbonate is much lower in RTA type 1 than in other types (HCO_3^- <10 mEq/L) because of impaired distal H+ secretion.

ETIOLOGY

May be due to genetic causes or acquired causes (obstructive uropathy, autoimmune disorders, amphotericin B, etc.).

SIGNS AND SYMPTOMS

- Clinical manifestation and severity depend on etiology.
- Presentation may include vomiting, dehydration, poor growth, nephrocalcinosis, and hypokalemia.

TREATMENT

Correct acidosis with bicarbonate therapy, as it is a chronic cause of metabolic acidosis.

TYPE 2—PROXIMAL RTA

PATHOPHYSIOLOGY

- Hyperchloremic metabolic acidosis usually without a high urinary pH (<5.5) due to decreased proximal tubular reabsorption of bicarbonate.

- Normal function of distal tubules allow acidification of urine. However, in severe cases this mechanism can be overwhelmed and urine pH may increase to >5.5.
- Increased sodium delivery to the distal tubule increases aldosterone secretion, leading to hypokalemia.

ETIOLOGY

- May occur as an isolated disorder or as a generalized defect in proximal tubular transport (Fanconi syndrome).
  - Isolated proximal RTA is rare in children.

SIGNS AND SYMPTOMS

Clinical presentation depends on the underlying etiology (see section on Fanconi syndrome).

TREATMENT

Correct acidosis with alkali replacement. Larger doses of alkali are needed for type 2 RTA due to bicarbonate loss via urine. Bicarbonate diuresis may also cause hypokalemia, which can be treated with potassium citrate.

TYPE 4—MINERALOCORTICOID DEFICIENCY RTA

PATHOPHYSIOLOGY AND ETIOLOGY

- Caused by aldosterone deficiency (congenital adrenal insufficiency, aldosterone synthase deficiency, medication, HIV) or aldosterone resistance (mineralocorticoid deficiency).
  - The most common cause of hypoaldosteronism in children is medication—NSAIDs, trimethoprim, heparin, potassium-sparing diuretics, etc.
  - Characterized by hyperkalemia, acidic urine—urinary pH <5.5 (distal tubule H^+ pump functions normally).

SIGNS AND SYMPTOMS

- Failure to thrive.
- Persistent hyperkalemia.
- Mild metabolic acidosis and hyponatremia.

TREATMENT

- Correct acidosis and any electrolyte imbalance.
- Replace any deficient hormones.

PROGNOSIS OF RTA TYPE 1,2, AND 4

- Distal RTA can be a lifelong disease and may lead to renal failure.
- Proximal RTA and mineralocorticoid RTA usually resolve within 12 months.

Fanconi Syndrome

DEFINITION

- Rare disorder characterized by generalized proximal tubular dysfunction with **hypophosphatemia**.
  - Loss of phosphate, glucose, amino acids, protein in urine, as well as proximal RTA (as above).

> **EXAM TIP**
>
> Type 1 and type 2 RTA are associated with **hypokalemia** due to aldosterone activation. Type 4 RTA is associated with **hyperkalemia** due to aldosterone deficiency or resistance.

ETIOLOGY

- Can be inherited or acquired.
- Inherited causes include the following:
  - Cystinosis, **galactosemia**, hereditary fructose intolerance, tyrosinemia type I, and Wilson disease.
- Acquired secondary to exposure to:
  - Drugs (ifosfamide, cisplatin, aminoglycosides, and valproic acid).
  - Heavy metals (lead, mercury, cadmium).

SIGNS AND SYMPTOMS

- Hypophosphatemia and low vitamin D commonly cause bony abnormalities (rickets/osteomalacia) and growth failure.
- Loss of ions causes polyuria and hypovolemia.
- Hypokalemia causes constipation and muscle weakness.

DIAGNOSIS

Metabolic abnormalities, including hypophosphatemia, hypokalemia, proteinuria, and hyperchloremic metabolic acidosis.

TREATMENT

See above section on proximal RTA.

Acute Kidney Injury (AKI)/Acute Kidney Disease (AKD)

> A 2-year-old boy develops bloody diarrhea a few days after eating in a fast-food restaurant. A few days later, he develops facial edema, pallor, lethargy, and decreased urine output. Blood work shows a low hematocrit and platelet count. A UA reveals blood and protein in the urine. *Think: Hemolytic uremic syndrome (HUS) secondary to* Escherichia coli *O157:H7 infection.*
>
> HUS is usually preceded by either gastroenteritis (usually diarrheal) or an upper respiratory tract infection. *E. coli* can be acquired by eating undercooked red meat or in some cases unwashed vegetables. Sudden onset of pallor, lethargy, and oliguria following an infection suggests HUS. Hemolytic uremic syndrome is characterized by hemolytic anemia, thrombocytopenia, and uremia from endothelial damage in small vessels like the kidney. The peripheral smear may show schistocytes and burr cells.

DEFINITION

- Formerly known as acute renal failure (ARF).
- Abrupt decline in renal function, reflected by acute rise in BUN (azotemia), serum creatinine, or both. Often transient, but always <3 months.
  - Acute kidney injury (AKI) is defined by increase in serum creatinine by 50% within 7 days or by 0.3 mg/dL within 2 days, or presence of oliguria.
  - Acute kidney disease (AKD) is defined as AKI or a decreased GFR <60 mL/1.73 m^2 (or by >35%) for <3 months. AKI is a subset of AKD.
- Three main types: prerenal, renal (intrinsic), and postrenal.
- Prerenal is the most common cause of AKI.

A 4-year-old boy develops oliguria 12 hours after operation for a ruptured appendix. Creatinine (Cr) is 0.5 mg/dL, blood urea nitrogen (BUN) is 23 mg/dL, urine sodium is 12 mEq/L. *Think: Prenatal AKI (or prerenal azotemia).*

Oliguria is most often due to dehydration. Historical features include vomiting, diarrhea, and poor oral intake. A BUN-to-serum creatinine ratio of >20:1 is suggestive of prerenal AKI. Other features are decreased concentration of urinary sodium, increased urinary excretion of creatinine, and a high urine osmolality. Note, however, that a normal or slightly elevated creatinine level does not exclude prerenal AKI. The precipitating event for prerenal AKI is renal hypoperfusion. Give normal saline for blood volume expansion. Reversibility with treatment of the underlying cause is the hallmark.

PATHOPHYSIOLOGY

- **Prerenal:**
  - Hypoperfusion of the kidneys secondary to blood loss, intestinal fluid loss, sepsis, heart failure, etc.
  - Gastroenteritis is the most common cause of hypovolemia.
  - Oliguria is always present.
  - Prolonged renal hypoperfusion can cause acute tubular necrosis (ATN), which is an irreversible intrinsic renal disease.
  - Potentially reversible if blood flow is restored prior to ATN.
- **Renal (Intrinsic):**
  - Renal parenchymal damage caused by the following:
    - Glomerular disease (e.g., poststreptococcal glomerulonephritis).
    - Vascular disease (e.g., hemolytic uremic syndrome).
    - Tubulointerstitial disease (secondary to drugs, UTIs, myoglobinuria from rhabdomyolysis).
  - The kidneys are unable to concentrate urine effectively.
- **Postrenal:**
  - Caused by any significant physical or functional obstruction of the urinary tract (posterior urethral valves, bilateral ureteropelvic or ureterovesical obstruction, renal stones, neurogenic bladder, medications).
  - Often associated with infection.
  - Prolonged obstruction can lead to intrinsic renal disease.

SIGNS AND SYMPTOMS

- Signs and symptoms vary by etiology but commonly include:
  - Oliguria or anuria, dysuria.
  - Edema.
  - Gross or microscopic hematuria.
  - Hypertension (HTN).

DIAGNOSIS

- Obtain a careful history to determine the cause of AKI.
- Catheterize the patient to monitor urine output and obtain urine studies.
- Serum and urine chemistry are useful tests for differentiating the cause.
  - Prerenal: BUN:Cr >20:1 with FeNa <1%.
  - Renal: BUN:Cr <20:1 and FeNa >1%.
- In intrinsic AKI, urinalysis may reveal proteinuria or hematuria. UA in prerenal AKI is normal. UA in postrenal AKI can be normal or have varying degrees of hematuria.
- In children with postrenal AKI, a renal ultrasound will show dilation of the renal pelvis and collecting system.

EXAM TIP

A common cause of AKI in toddlers is hemolytic-uremic syndrome (HUS).

WARD TIP

AKI may be due to pre-renal, renal (intrinsic), or post-renal causes.

WARD TIP

Normal urinary output: 1–4 mL/kg/hr.

WARD TIP

Oliguria
Infants: <1 mL/kg/hr for more than 6 hours
Older children: <0.5 mL/kg/hr for more than 6 hours

WARD TIP

Prerenal: BUN:Cr >20:1 with FeNa <1%
Renal: BUN:Cr <20:1 and FeNa >1%

TREATMENT

- Treat patients with hypovolemia (as in prerenal AKI) with volume replacement and monitor I/Os to prevent worsening AKI.
- For patients with oliguria leading to hypervolemia, treat with fluid restriction and/or furosemide. In critically ill patients with intrinsic AKI, consider dialysis.
- Monitor and treat electrolyte imbalances (hyperkalemia, metabolic acidosis).
- Avoid drugs that can precipitate or worsen AKI (NSAIDs, contrast dyes) in patients with decreased renal perfusion. Adjust the dosing of any renally excreted medications.

COMPLICATIONS OF AKI

AKI can lead to chronic kidney disease (>3 month) and can have profound electrolyte abnormalities. See CKD section for more information.

Chronic Kidney Disease (CKD)

On a routine exam, a 10-year-old girl has HTN of 160/90 in all extremities. *Think: Renal disease.*
BP should be measured at least twice with appropriate cuff size. A short or narrow cuff may artificially raise BP measurement. Renal parenchymal disease and coarctation of the aorta are common causes of hypertension in children 1–10 years of age. Coarctation of the aorta would present with a higher BP in the upper extremities, while renal disease presents with consistent BP readings throughout. The most appropriate next test is UA.

DEFINITION

- CKD is a result of irreversible kidney damage, which may lead to end-stage renal failure.
- GFR <60 mL/min per 1.73 m^2 for >3 months.

OR

- GFR >60 mL/min per 1.73 m^2 with evidence of structural damage or functional kidney abnormalities (pathologic abnormalities on histology, proteinuria, casts, renal tubular disorders, imaging abnormalities, etc.).

ETIOLOGY

- Most commonly due to congenital abnormalities—obstructive uropathy, hypoplastic or dysplastic kidneys, reflux nephropathy, polycystic kidney disease.
- Focal segmental glomerulosclerosis is the most common glomerular disease seen in patients with CKD.
- Diverse etiologies can cause initial damage to the kidney. The kidney then compensates by adaptive hyperfiltration. Adaptive hyperfiltration and/or repeated insults due to the primary disease may cause further glomerular damage to the remaining nephrons. The cycle repeats and causes progressive renal insufficiency.
- **CKD Staging per KDIGO guideline for children >2 years-old**

	GFR Range (mL/min/1.73 m^2)
G1 (Normal)	≥ 90
G2	60–89
G3	30–59
G4	15–29
G5 (ESRD)	**<15**

Signs and Symptoms

- Asymptomatic in the early stages with gradual symptom onset. May have polyuria, or nocturia.
- Patients may also develop headache, fatigue, lethargy, anorexia, nausea, vomiting, polyuria, and growth failure. In cases of glomerular disorders, proteinuria, discolored urine, and edema may accompany other findings.

Complications

- HTN: Renin-angiotensin-aldosterone system stimulated by diminished GFR.
- Anemia: Due to decreased kidney erythropoietin production.
- Electrolyte imbalances including:
  - Hyperkalemia: Secondary to impaired renal tubule function and renal tubular acidosis (ion shifts due to acidosis).
    - A serum potassium level >6.5 mEq/L can lead to arrhythmias and must be treated emergently. Give calcium gluconate to stabilize the myocardium, sodium bicarbonate, glucose and insulin, Kayexalate (sodium polystyrene), and albuterol.
- Metabolic acidosis: Due to hyperuricemia.
  - **Hypocalcemia** may result from the kidney's inability to hydroxylate vitamin D into an active form, which is responsible for GI absorption of calcium.
    - To compensate for low calcium, **hyperparathyroidism** may occur, which can cause bone loss and lead to growth impairment.
  - **Hyperphosphatemia** occurs due to the kidney's inability to excrete phosphate and causes itching.
  - **Hyponatremia** may result secondary to excessive administration of hypotonic fluids to oliguric patients. Patients with a serum sodium <120 are at risk for developing cerebral edema and central nervous system (CNS) hemorrhage. Partial correction should be undertaken to raise the Na level to at least 120 mEq Na.
- Dyslipidemia: Lipid metabolism is abnormal in patients with CKD, and there is increased risk for cardiovascular disease.
- See Table 14-1 for a listing of symptoms of uremia.

WARD TIP

Cardiac arrest from hyperkalemia is a life-threatening complication of AKI/CKD.

WARD TIP

Correcting hyponatremia too rapidly (>9 mEq/L in 24 hours) can lead to central pontine myelinolysis due to severe damage neurons in the pons. This can cause paralysis, difficulty speaking and swallowing, and other neurologic symptoms.

TABLE 14-1. Symptoms of Uremia

Azotemia (accumulation of nitrogen products)
Acidosis
Sodium wasting
Sodium retention
Urinary concentrating defect
Hyperkalemia
Renal osteodystrophy
Growth retardation
Anemia
Bleeding tendency
Infection
Neurologic (fatigue, poor concentration, headache, drowsiness, muscle weakness, seizures, coma)
Gastrointestinal ulceration
Hypertension
Hypertriglyceridemia
Pericarditis and cardiomyopathy
Glucose intolerance

TREATMENT

- Address the underlying etiology, treat any reversible kidney damage to slow the progression of CKD, and treat symptoms and complications.
  - Growth failure is a prominent complication of CKD: Ensure adequate caloric intake. Recombinant human growth hormone therapy can improve linear growth.
  - HTN: Strict BP control with ACE inhibitors or ARBs.
  - Anemia: Treat with iron supplementation and erythropoietin.
  - Bone disorders: Treat secondary hyperparathyroidism by normalizing the serum calcium and phosphorus levels with calcium supplements and phosphate binders, and vitamin D replacement.
  - Address any other fluid and electrolyte imbalances.
- **Renal replacement therapy** (e.g., transplant, dialysis) is necessary for patients with GFR <15. In children, it may be considered earlier (GFR <30).

End-Stage Renal Disease (ESRD)

An 8-year-old patient receiving peritoneal dialysis for ESRD develops abdominal pain and fever. *Think: Peritonitis.*

The most serious complication of peritoneal dialysis is peritonitis. It should be suspected in dialysis patients with abdominal pain and fever. Common causative organisms are coagulase-negative staphylococci, *S. aureus*, streptococci, *Escherichia coli*, *Pseudomonas*, and other gram-negative organisms.

DEFINITION

The last stage of the CKD, when the kidney function becomes irreversibly compromised and the GFR falls below 15 mL/min/1.73 m^2.

TREATMENT

- Renal replacement therapy is necessary at GFR <15. RRT may be initiated earlier in children to allow adequate nutrition and normal growth.
- **Dialysis:** No significant difference in outcomes has been shown between hemodialysis (HD) and peritoneal dialysis (PD). Mode of dialysis should be chosen based on contraindications and the patient/family's preference.
  - Infants and younger children may prefer PD due to certain advantages (less restrictive diet, therapy performed at home, no repeated venipuncture, etc.).
  - Hemodialysis should be performed in children with contraindications to PD (intra-abdominal pathology, etc.).
- **Renal transplant:** Renal transplantation is the preferred mode of treatment for most children with ESRD.
  - Contraindications for transplant include metastatic malignancy, systemic sepsis, elevated anti-GBM antibodies, severe multi-organ failure, extra-renal disorder not correctable by renal transplant, and other contraindications to surgery. HIV infection is no longer an absolute contraindication for transplantation.

Hypertension

DEFINITION

Hypertension in children is defined as systolic and/or diastolic BP above the 95th percentile, measured on ≥3 separate occasions. Normal range for BP depends on age, gender, and height.

ETIOLOGY

- In older children (above age 15), primary HTN is the most common cause of HTN.
  - Risk factors include obesity, male gender, African American ethnicity, family history.
- In younger children (below age 15), HTN is most likely due to a secondary cause.
  - Renal parenchymal disease (glomerulonephritis, polycystic kidney disease, CKD).
  - Endocrine disease (thyroid disease, corticosteroid excess, catecholamine-producing tumors).
  - Renovascular disease (fibromuscular dysplasia, renal artery hypoplasia).
  - Cardiac disease (coarctation of aorta).
  - Drugs.

DIAGNOSIS

- Initially, BP should be obtained from all four extremities.
- Careful history and physical to determine primary versus secondary etiology.
- Initial testing should include BMP, CBC, UA, renal US, and echocardiogram.
- Mild HTN and no comorbidities: Recommend lifestyle changes.
- More severe HTN or comorbidities (renal disease, end-organ damage, diabetes, etc.): Initiate pharmacologic treatment. Thiazide diuretics, ACEi, CCBs, and beta-blockers are most often used in children.
- Secondary HTN: Address the underlying etiology.

Proteinuria

APPROACH

- Proteinuria up to 150 mg/day may be normal (can be higher in neonates).
- Transient proteinuria: Most common cause, can be induced by many factors including fever, exercise, and seizures.
- Orthostatic/postural proteinuria: Increased protein excretion in upright position, which returns to normal when patient is lying down. Especially common in adolescent males.
- Persistent proteinuria should be evaluated for a glomerular lesion.

> **WARD TIP**
>
> Nephrotic range proteinuria = Protein excretion of >40 mg/m^2/hr. Random urine protein/creatinine ratio >3.0.

Glomerular Diseases (Nephrotic and Nephritic Syndromes)

- Glomerular disorders are often classified as causes of nephrotic syndrome, nephritic syndrome, or both.

NEPHROTIC SYNDROME	OVERLAP	NEPHRITIC SYNDROME
Minimal Change Disease	**Membranoproliferative Glomerulonephritis**	**Poststreptococcal Glomerulonephritis**
Focal segmental Glomerulosclerosis		Rapidly progressive Glomerulonephritis
Membranous Nephropathy		**IgA nephropathy (Berger's)**
		Alport syndrome

- Nephrotic and nephritic (glomerulonephritis) syndromes will be defined, and diseases in bold will be elaborated further.

Nephrotic Syndrome

A 2-year-old boy has a 1-week history of edema. On examination, he is normotensive with generalized edema and ascites. Lab values show Cr 0.4 (normal), albumin 1.4 g/dL, and cholesterol 569 mg/dL. A UA shows 4+ protein and no blood. *Think: Nephrotic syndrome.*

The common age of presentation is 2–6 years. Minimal change disease is the most common nephrotic syndrome in children. Periorbital and peripheral edema is typically present. Histopathologic examination shows no glomerular abnormalities on light microscopy in minimal change disease.

DEFINITION

- Nephrotic syndrome is caused by renal diseases that increase the permeability across the glomerulus. It is characterized by the following:
  - Nephrotic range proteinuria (>40 mg/kg/day).
  - Hypoalbuminemia (serum level <3g/dL).
  - Edema.
  - Hyperlipidemia.

ETIOLOGIES

- Minimal change disease—the most common nephrotic syndrome in children.
- Focal segmental glomerular sclerosis (FSGS).
- Membranous nephropathy.
- Nephrotic syndrome can also be secondary to systemic illnesses such as lupus and Henoch-Schönlein purpura.

PATHOPHYSIOLOGY

- Permeability across the glomerular capillary wall is normally regulated by charge selectivity (negatively charged to prevent passage of anions) and size selectivity. In nephrotic syndrome this barrier is disrupted.
- In minimal change disease, there is loss of anionic charge in the glomerular capillary wall with no structural damage visible on light microscopy.

EPIDEMIOLOGY

Primary nephrotic syndrome most common in children between 2 and 6 years of age, and commonly follows a viral upper respiratory infection.

SIGNS AND SYMPTOMS

- Edema is the most common presenting symptom for all nephrotic syndromes.
  - Often initially periorbital edema, usually pitting, can become as severe as anasarca (generalized massive total body edema).
- Nonspecific complaints such as malaise, headache, fatigue, and irritability common.
- +/− Hematuria depending on etiology of nephrotic syndrome (much more likely if secondary to glomerulonephritis).
- Labs show nephrotic range proteinuria (>40 mg/kg/day) and hypoalbuminemia (serum level <3 g/dL), and hyperlipidemia.

DIAGNOSIS

- The diagnosis is usually made clinically, with supportive lab values.
- Patients are empirically treated with steroids. As the majority of patients with nephrotic syndrome have MCD, most will respond. Patients who don't respond will need renal biopsy.

TREATMENT

- Over 90 percent of children with minimal change disease will respond to steroids (4–6 weeks of prednisone).
- In the case of relapse, steroids remain the first-line agent.
- In the case of significant side effects due to steroids (such as growth impairment and weight gain) other available agents include cyclophosphamide, cyclosporine, mycophenolate mofetil, and rituximab.
- For other etiologies of nephrotic syndrome such as FSGS and membranous nephropathy, steroids remain first-line treatment, although response is usually poor with progression to CKD.

COMPLICATIONS

- Infection is common due to loss of immunoglobulins in the urine. URI, UTI, and spontaneous bacterial peritonitis are the three most frequent infections.
  - In spontaneous bacterial peritonitis, two most common organisms are *Streptococcus pneumoniae* and *Escherichia coli*.
- Thromboembolism: Hypercoagulability due to thrombocytosis and decreased levels of antithrombin III, plasminogen, and protein S (urinary loss).
  - Renal vein thrombosis, deep vein thrombosis, and pulmonary embolism.
- Renal Insufficiency: Can progress to end-stage renal disease especially in those who are steroid-resistant.
- Anasarca.
- Hypovolemia: Despite markedly increased extracellular fluid volume, children can present with third spacing of fluid and signs of decreased effective circulating volume (tachycardia, oliguria, peripheral vasoconstriction).

Glomerulonephritis (GN)

Causes of gross hematuria:
- Urinary tract infections
- Trauma
- Irritation of urethral meatus
- Nephrolithiasis
- Sickle cell disease/trait
- Coagulopathy
- Glomerular disease
- Malignancies
- Drug-induced hemorrhagic cystitis (cyclophosphamide)

DEFINITION

- Group of diseases that cause glomerular injury via inflammation.
- Causes nephritic syndrome.

CLINICAL SYMPTOMS

- Edema.
- Gross hematuria.

WARD TIP

Can begin steroid therapy for MCD without renal biopsy in patients who:
- Are >1 years old and <12 years old
- Have symptoms of nephrotic syndrome
- None of the following present:
  - Hypertension
  - Gross hematuria
  - Marked serum creatinine elevation
  - Abnormal serum complement levels
- If any of the above findings are present, this suggests an alternative etiology than minimal change disease

---

EXAM TIP

Urine dipstick is not an accurate measure of protein excretion. Obtain a urine protein/creatinine ratio.

WARD TIP

In **membranous nephropathy**, immune complexes deposit in the glomeruli and cause nephrotic syndrome. Although it is the most common cause of nephrotic syndrome in adults, it is uncommon in children. Microscopy can cause deposits of IgG and C3. It is associated with lupus, hepatitis B, and hepatitis C.

- Hypertension.
- +/– Proteinuria (less than nephrotic range proteinuria).

DISEASE COURSE

- Acute glomerulonephritis— sudden onset hematuria +/– mild proteinuria, decreased GFR, and retention of sodium and water leading to hypertension and edema.
  - Most commonly caused by poststreptococcal glomerulonephritis (PSGN).
- Rapidly progressive glomerulonephritis (RPGN)–features of acute GN and progressive loss of renal function over relatively short period of time.
  - Rare in children, can be from any cause of glomerulonephritis.
  - Presence of crescent-shaped scars in the majority of the glomeruli.
  - Treatment with steroids, cyclophosphamide or rituximab, and in some cases plasmapheresis, but prognosis is typically poor with most patients requiring dialysis.
- Chronic glomerulonephritis: Patients often present with asymptomatic hematuria or proteinuria but can also present as acute glomerulonephritis and progress to CKD.

Poststreptococcal Glomerulonephritis (PSGN)

A 4-year-old girl presents with malaise, generalized edema, and red-brown colored urine. She had a strep throat infection 2 weeks prior. C3 level is decreased, and an antistreptolysin O (ASO) titer is positive. *Think: PSGN.*

PSGN occurs after an infection of the throat or skin by a nephritic strain of group A beta-hemolytic streptococci. It is manifested as an acute nephritic syndrome or as isolated hematuria. It is mediated by immune complexes, which is suggested by the low complement level.

DEFINITION

- Acute glomerulonephritis mediated by immune complex deposition induced by group A beta-hemolytic streptococcus.
- Typically occurs following GAS pharyngitis or skin infection (impetigo).

EPIDEMIOLOGY

- Most common cause of acute glomerulonephritis globally, but primarily in developing countries.
- 2:1 male-to-female ratio, increased risk in ages 5–12.

SIGNS/SYMPTOMS

Most common presenting symptoms are edema, gross hematuria, hypertension +/– proteinuria.

DIAGNOSIS

- Based on clinical findings and evidence of recent Group A strep infection:
  - Renal function: Variable decline in GFR, can see rise in serum Cr.
  - Positive throat cultures or antibody titers to streptococcal antigen.
  - UA: RBC casts, RBCs, varying amounts of protein, sometimes pyuria.
  - Serum complement: Low C3 in first 2 weeks of illness, resolves within 4–8 weeks.
  - Renal biopsy: Typically not needed as PSGN tends to begin to resolve within 1 week of presentation.

TREATMENT AND PROGNOSIS

- Treatment is primarily supportive.
- Monitor for hypertension and pulmonary edema. Treat with sodium and water restriction and loop diuretics if needed.
- Treatment with penicillin will not prevent PSGN but can help prevent development of rheumatic fever.
- Treat renal failure or life-threatening fluid overload with peritoneal dialysis.
- Microscopic hematuria usually resolve within 3–6 months.
- Proteinuria clears more slowly; mild increase in protein excretion can still be present up to 10 years later.

A patient presents with hemoptysis, sinusitis, and glomerulonephritis. *Think: Granulomatosis with polyangiitis* (formerly called Wegener's granulomatosis).

Granulomatosis with polyangiitis is a systemic vasculitis involving the upper and lower airways and kidneys. It is rare before adolescence. Features include necrotizing granulomatous lesions in the upper and lower respiratory tracts, necrotizing vasculitis, and focal glomerulonephritis. Most patients present with respiratory symptoms. Patients are typically c-ANCA positive. The radiographic findings may include nodular infiltrates, pulmonary nodule, cavitation, and diffuse alveolar hemorrhage.

Membranoproliferative Glomerulonephritis

DEFINITION

- Pattern of glomerular injury on renal biopsy characterized by mesangial hypercellularity and basement membrane thickening. It is often described as having a "tram-track" pattern.
- May present with nephrotic and/or nephritic syndrome.
- Two primary mechanisms:
  - Immune complex deposition leading to activation of complement.
  - Dysregulation and persistent activation of complement pathway.

ETIOLOGIES

Associated with infections (HBV/HCV, chronic bacterial/fungal infections), autoimmune diseases (Sjögren's, SLE), monoclonal gammopathies, etc.

SIGNS AND SYMPTOMS

Varied presentation including nephrotic syndrome, nephritic syndrome, microscopic hematuria +/– proteinuria.

DIAGNOSIS

- Made with renal biopsy.
- Serum complement levels often low.

TREATMENT AND PROGNOSIS

- Treat any underlying cause if present.
- Poor prognosis especially in patients with nephrotic syndrome, elevated serum creatinine, hypertension, or RPGN on renal biopsy. Often progresses to CKD.
- There is no definitive therapy, although some patients respond to steroids.

> 👤 A patient presents with dyspnea, hemoptysis, and AKI. *Think: Goodpasture syndrome.*
>
> Goodpasture syndrome is an antiglomerular basement membrane disease. Triad: Glomerulonephritis, pulmonary hemorrhage, and antibody to basement membrane antigens. Respiratory manifestations: Cough, dyspnea, and hemoptysis associated with pulmonary hemorrhage. Renal manifestations: Acute nephritic syndrome with hematuria, proteinuria, and HTN. UA may show active sediment with RBCs and RBC casts.

IgA Nephropathy (Berger Disease)

DEFINITION

Glomerulonephritis thought to be caused by deposition of IgA (often complexed with C3 and IgG) in the mesangium and along glomerular capillary wall.

EPIDEMIOLOGY

- Most common cause of acute glomerulonephritis throughout developed world.
- Most common in second and third decades of life but can present at any age.

SIGNS AND SYMPTOMS

- Typically follows an upper respiratory tract infection.
- 40–50% present with one or recurrent episodes of gross hematuria.
- 30–40% have microscopic hematuria and mild proteinuria and detected incidentally.
- <10% present with nephrotic syndrome or acute RPGN with edema, hypertension, and renal insufficiency.

DIAGNOSIS

- Suspicion generally based on clinical history and lab data.
- Can only be confirmed with renal biopsy with immunofluorescence studies for IgA deposits.
    - Identical to renal biopsy findings seen in Henoch-Schönlein purpura, since both are caused by IgA deposition.
- Biopsy only performed if signs of more severe or progressive disease (excessive proteinuria, elevated creatinine).

TREATMENT

- Can be benign, but slow progression to ESRD occurs in up to 50% of affected patients over 20–50 years.
- ACE inhibitors or ARBs for blood pressure control and to slow renal disease progression.
- Steroid therapy only for patients with declining GFR, persistent proteinuria despite ACEi/ARB therapy or evidence of active disease on renal biopsy.
- Renal replacement therapy if progression to CKD or ESRD.

Alport Syndrome

DEFINITION

Also called hereditary nephritis–inherited glomerular disease associated with sensorineural hearing loss and ocular abnormalities.

WARD TIP

Henoch-Schönlein purpura is a systemic disease that typically affects children and is often preceded by a throat infection. It is a small vessel vasculitis that can cause purpuric rash on the lower extremities and other symptoms. In the kidneys, deposition of IgA and C3 can cause hematuria and proteinuria. Although renal biopsy is the same as IgA nephropathy, HSP is a systemic disease and IgA nephropathy only affects the kidneys.

WARD TIP

IgA nephropathy is a common cause of gross hematuria, seen most often in young adults.

SIGNS AND SYMPTOMS

- Initial renal manifestation is asymptomatic, persistent microscopic hematuria.
- Over time proteinuria, hypertension, and progressive renal insufficiency develop.

DIAGNOSIS

- Generally suspected from family history of deafness and renal failure.
- Can be confirmed by skin or renal biopsy or molecular genetic testing.

TREATMENT

No specific treatment currently available, renal transplant for renal failure (disease does not occur in transplanted kidney).

> **WARD TIP**
>
> Suspect Alport syndrome in patients with deafness and a family history of renal failure.

Systemic Lupus Erythematosus (SLE)

DEFINITION

- A systemic autoimmune disease that can affect skin, joints, kidneys, lungs, nervous system and other organ systems.
  - The most common initial symptoms are fever, weight loss, and malaise over several months.

PATHOPHYSIOLOGY

- Clinical manifestations are mediated by autoantibody formation and immune complex deposition.
- Immune complexes deposit in the glomeruli, which activates complement, causing renal dysfunction.
- See Table 14-2 for classification.

EPIDEMIOLOGY

- Most common in adolescent females.
- Can occur at any age. Incidence increases after 5 years of age and even further after the first decade.

T A B L E 1 4 - 2 . **SLE Nephritis—World Health Organization (WHO) Classification and Symptoms**

CLASSIFICATION	HISTOPATHOLOGY	SYMPTOMS
Class I	No histologic abnormalities detected.	No symptoms
Class II	Mesangial lupus nephritis. Glomeruli have mesangial deposits containing immunoglobulin and complement.	Hematuria Normal renal function Proteinuria of < 1 g/24 hr
Class III	Focal segmental lupus glomerulonephritis. Mesangial deposits in all glomeruli and subendothelial deposits in some.	Hematuria ± Proteinuria ± Reduced renal function ± Nephrotic syndrome
Class IV	Diffuse proliferative lupus nephritis. All glomeruli contain massive mesangial and subendothelial deposits of immunoglobulin and complement.	Hematuria ± Proteinuria ± Reduced renal function ± Nephrotic syndrome
Class V	Membranous lupus nephritis. Resembles idiopathic membranous glomerulopathy.	Nephrotic syndrome

SIGNS AND SYMPTOMS

- See Table 14-2 for symptoms of various stages of lupus nephritis.
- Renal disease (lupus nephritis) is more frequent early in the disease course in children and is often more severe.

DIAGNOSIS

- Specific ACR classification criteria.
- Antinuclear antibodies (ANA) are highly sensitive, whereas anti-Smith antibodies and anti-double-stranded DNA antibodies (anti-dsDNA) are highly specific for SLE.
- Markers of disease activity:
    - Anti-double-stranded DNA.
    - Low complement levels C3 and C4 during active disease.

TREATMENT

- Immunosuppressive therapy (e.g., prednisone, azathioprine, hydroxychloroquine) to help reduce/prevent flare-ups but cannot cure the disease.
- Mycophenolate mofetil and rituximab are used in more severe/refractory cases of lupus nephritis.

Acute Interstitial Nephritis

DEFINITION

Inflammation in the interstitium between the glomeruli in the areas surrounding the tubules.

RISK FACTORS

- Reaction to medications (NSAIDs, penicillin, cephalosporins, sulfonamides, ciprofloxacin, cimetidine, PPIs, rifampin, thiazides, furosemide, allopurinol) is the most common cause.
- Infections (especially in children).
- Systemic diseases (SLE, Sjögren's, and sarcoidosis).

SIGNS AND SYMPTOMS

- Regardless of the cause, patients present with nonspecific signs/symptoms of acute renal dysfunction including nausea, vomiting, and malaise, but also can be asymptomatic.
    - Oliguria can be seen. Gross hematuria and proteinuria are very rare.
- In drug-induced AIN, one or more of the classical triad of rash, fever, and eosinophilia may also be present, although not necessary for diagnosis.

DIAGNOSIS

- Suspect if elevated serum creatinine, or urinalysis shows WBCs, WBC casts, and possibly eosinophiluria.
- Renal biopsy demonstrates interstitial edema and marked interstitial infiltrate of inflammatory cells.

TREATMENT

- Remove offending agent if drug-induced.
- Immunosuppressive therapy with steroids is sometimes used.
- Prognosis is variable.

WARD TIP

Classic triad in acute interstitial nephritis is rash, fever, and eosinophilia.

Renal Parenchymal Malformations

- **Renal dysplasia:** Abnormal differentiation of embryonic cells resulting in abnormal structure and decreased number of nephrons and presence of nonrenal tissues (cartilage and bone). Can affect all or part of the kidney.
- **Renal hypoplasia:** Nondysplastic small kidney that has decreased number but structurally normal calyces and nephrons.
- **Renal hypodysplasia:** Congenitally small kidney with dysplastic features.

A 1-week-old male newborn has a wrinkled abdomen that lacks anterior abdominal musculature. He also has clubfeet and is in respiratory distress. His bladder is distended and easily palpable, and neither testis is in his scrotum. Lab findings include BUN 30, Cr 2, and HCO3 15. *Think: Prune belly syndrome.*

Triad: Absent abdominal wall muscles, undescended testes, and **renal dysplasia**. The renal collecting system is dilated and nephrons are incompletely differentiated. Abnormalities of bladder, testicles, prostate, and/or ureter are common. Respiratory distress may be present due to pulmonary hypoplasia secondary to severe oligohydramnios.

Renal Agenesis

DEFINITION

- Congenital absence of renal parenchymal tissue, may be unilateral or bilateral.
  - Bilateral renal agenesis is incompatible with life.
  - Children with a solitary kidney are at increased risk for long-term CKD, thought to be due to glomerular hyperfiltration.
  - Diagnosis should prompt evaluation for associated abnormalities such as chromosomal anomalies and VACTERL association (vertebral anomalies, anal atresia, cardiac defects, TE fistula, renal defects, limb defects).

WARD TIP

VACTERL Association should be suspected with congenital renal abnormalities:
- Vertebral anomalies
- Anal atresia
- Cardiac defects
- TE fistula
- Renal defects
- Limb defects

Polycystic Kidney Disease (PKD)

An 8-month-old girl has an easily palpable kidney. US shows cystic kidneys, hepatic fibrosis, and portal HTN. *Think: Autosomal-recessive polycystic kidney disease.*

Classic presentation: Bilateral flank masses during the neonatal period or early infancy. US may show uniformly hyperechogenic kidneys. Presence of hepatic fibrosis supports this diagnosis.

DEFINITION

- An inherited disorder that causes bilateral renal cysts without dysplasia.
- Two types: Autosomal-dominant PKD (ADPKD) and autosomal-recessive PKD (ARPKD).

ADPKD

PATHOPHYSIOLOGY

- Previously known as infantile polycystic kidney disease.
- Caused by mutations in the PKHD1 gene, which encodes for fibrocystin.

- Primarily affects the kidney and the hepatobiliary tract.
  - Enlarged kidneys with numerous microcysts (cystic dilatations of the collecting ducts) that radiate from the medulla to the cortex. No obstruction of the urinary flow, but progressive disease causing larger cysts and interstitial fibrosis can cause renal dysfunction.
  - Biliary dysgenesis that leads to congenital hepatic fibrosis and dilatation of the intrahepatic bile ducts. This results in hepatomegaly and portal HTN over time.

SIGNS AND SYMPTOMS

- May be detected prenatally by ultrasound in severe cases.
- In severe cases, neonates will present with respiratory distress and/or other features of the Potter syndrome (flat nose, recessed chin, low-set ears, limb abnormalities, pulmonary hypoplasia).
- In less severe cases, infants or older children will present with progressively deteriorating renal function, portal HTN, and increased risk of cholangitis.

DIAGNOSIS

Diagnosed with abdominal ultrasound, which reveals enlarged hyperechogenic kidneys with poor corticomedullary differentiation and hepatobiliary disease.

TREATMENT

- Supportive.
- Renal replacement therapy for children who progress to ESRD.

> **WARD TIP**
>
> ARPKD—innumerable tiny cysts
> ADPKD—large cysts

ADPKD

PATHOPHYSIOLOGY

- Previously known as adult polycystic kidney disease.
- Caused by mutations in PKD1 or PKD2 gene, which encodes for polycystin 1 and polycystin 2, respectively.
- Characterized by macrocysts (large cystic dilatations in all parts of the nephron including all tubular segments and the Bowman's capsule).
- Complications commonly seen in adults such as cysts in the liver/pancreas or cerebral AV malformations are rare in children.

SIGNS AND SYMPTOMS

- Commonly presents in adulthood, but may present in childhood.
- Even if cysts develop early, most patients remain asymptomatic until adulthood.
- May present with gross or microscopic hematuria, proteinuria, infection of the cyst, HTN, and abdominal, flank, or back pain.
- Renal insufficiency can occur during childhood but is rare.

DIAGNOSIS

- Family history is helpful for diagnosis.
- Diagnosed with renal ultrasound, which reveals cysts.

> **WARD TIP**
>
> The most common cause of end-stage renal disease in children is congenital renal anomalies.

TREATMENT

- Supportive (BP control, pain management, treatment for UTI, etc.).
- Renal replacement therapy for patients who develop ESRD.

Horseshoe Kidney

DEFINITION

- Midline fusion of the lower kidney poles.
- Typically do not ascend fully due to tethering by inferior mesenteric artery and are found in the pelvis or lower lumbar vertebral levels.
- Majority of patients are asymptomatic.

ASSOCIATED CONDITIONS

- Urologic and genital anomalies are commonly found (e.g., vesicoureteral reflux, ureteropelvic junction obstruction, bicornuate uterus, hypospadias, and undescended testis).
- Horseshoe kidney can be a feature of many syndromes including Turner syndrome and common Trisomy syndromes (13, 18, and 21).
- There also appears to be an increased risk for developing Wilms tumor.

Wilms Tumor

A previously healthy 2-year-old boy has a left-sided abdominal mass discovered by his mother. His physical examination reveals a BP of 110/70 and a large mass arising in his left abdomen. A UA shows 5–10 erythrocytes and 2–3 leukocytes. *Think: Wilms tumor.*

The usual presentation of Wilms tumor is an abdominal mass, and it is not uncommon for the parent to discover this mass. It is often asymptomatic. The most appropriate next diagnostic test is an ultrasound of the abdomen and urinary tract. Because Wilms tumor metastasizes to the lungs, a chest radiograph should be obtained.

DEFINITION

- The most common renal malignancy in children.
- Also called nephroblastoma.
- Median age of diagnosis is 3.5 years.

PATHOPHYSIOLOGY

- Derived from the embryonic renal precursor cells (mesenchymal cells) that fail to undergo normal differentiation.
- Associated with gene mutations responsible for normal renal and genitourinary development.
- Certain mutations are associated with other syndromes that are frequently observed with Wilms tumor.
  - WT1 deletion is associated with the WAGR syndrome (Wilms tumor, Aniridia, GU anomalies, mental retardation).
  - Mutations in the 11p15.5 region (WT2) is associated with Beckwith-Wiedemann syndrome (macrosomia, macroglossia, hemihypertrophy, Wilms tumor, hepatoblastoma).

SIGNS AND SYMPTOMS

- Most commonly presents with an isolated abdominal/flank mass that rarely crosses the midline (as opposed to neuroblastoma).
- If present, symptoms include abdominal pain, hematuria, fever, and HTN due to obstruction of renal artery.

> **WARD TIP**
>
> The characteristic features of Beckwith-Wiedemann syndrome include omphalocele, macroglossia, and macrosomia. Also notable are the presence of hemihypertrophy (asymmetric growth), neonatal hypoglycemia, and increased risk for embryonal tumors, including Wilms tumor.

- Mostly solitary, but can be bilateral (5–7%) or multifocal within a single kidney (10%).
- May metastasize to lung, liver, bone, and brain.

DIAGNOSIS

- Renal ultrasound (US) is the initial imaging study. It may show hydronephrosis and echogenic intrarenal masses that may contain cystic areas.
- CT or MRI should follow renal US to determine the origin and extent of the tumor spread.
- Chest imaging is necessary to determine the presence of lung metastases.
- Definitive diagnosis and cell type determination are made by histologic confirmation after surgical excision or surgical biopsy. Transcutaneous biopsy is not recommended because it can spill tumor cells into the abdomen.

TREATMENT

- Depends on the stage and cell type of the tumor.
- In general, low-stage tumors are treated with nephrectomy and chemotherapy. High-stage or high-risk tumors may require additional radiation therapy.
- Stage 5 (bilateral) tumors are treated with preoperative chemotherapy followed by renal parenchymal-sparing surgical resection of the tumor.
- Long-term follow-up is necessary for prompt detection of tumor recurrence or any long-term complications.

Renal Vein Thrombosis (RVT) in Infancy

DEFINITION

- Thrombus formation in the renal vein.
- A common cause of venous thromboembolism during the neonatal period.
- Risk factors include:
  - Prematurity (especially with history of umbilical vein catheter), perinatal asphyxia, shock, dehydration, sepsis, polycythemia, cyanotic heart disease, maternal diabetes, and inherited prothrombotic conditions.
  - In older children, RVT is associated with nephrotic syndrome, burns, systemic lupus erythematosus, or renal transplant.

SIGNS AND SYMPTOMS

- Most often, insidious onset with no symptoms referable to the kidney.
- Can see gross hematuria, proteinuria, anuria, thrombocytopenia, vomiting, and hypovolemia.

DIAGNOSIS

- US shows swollen and echogenic kidneys.
- Doppler flow studies may show absent intrarenal and renal venous flow.
- Coagulation studies and prothrombotic disorder workup may be obtained on a case-by-case basis.

TREATMENT

- Correction of fluid and electrolyte abnormalities.
- Unilateral renal vein thrombosis without compromised renal function or extension into the IVC can be managed with supportive care.
- If there is extension into the IVC, compromised renal function or bilateral thrombosis, anticoagulate with unfractionated heparin.

Nephrolithiasis

An 8-year-old boy presents with left flank pain radiating to his left testicle. The pain does not change with movement or positioning and is colicky in nature. Urine dip is positive for blood. *Think: Nephrolithiasis.*

The pain begins in the flank, extends around the abdomen, and may radiate into the groin. Ipsilateral costovertebral tenderness may be present. Children with a history of multiple UTIs may be at risk of renal stones. UA typically shows hematuria, but absence of hematuria does not exclude the diagnosis of nephrolithiasis.

EPIDEMIOLOGY

- Lower incidence in children than in adults, with increased number occurring after 12.
- In most children, associated with metabolic abnormalities, urinary tract abnormalities, or urinary tract infection.

ETIOLOGY

- Made of calcium oxalate, calcium phosphate, struvite, uric acid, or cystine that accumulates in the calyx or bladder.
- Calcium stones:
  - Radiopaque, envelope-shaped stones.
  - Secondary to hypercalciuria due to increased intestinal absorption, decreased renal reabsorption, or increased bone resorption.
- Struvite stones:
  - Radiopaque, coffin-lid shaped stones composed of magnesium, ammonium, and phosphate.
  - Most commonly secondary to UTIs by urease-producing bacteria such as *Proteus*, and *Klebsiella*.
- Uric acid stones:
  - Rare in children.
  - Radiolucent, rhomboid-shaped stones associated with high serum uric-acid levels, such as in idiopathic hyperuricosuria, Lesch-Nyhan syndrome, chemotherapy (tumor lysis syndrome), and myeloproliferative disorders.
- Cystine stones:
  - Radiopaque, hexagonal-shaped stones associated with cystinuria, an autosomal-recessive disorder causing excessive excretion of dibasic amino acids (cystine, lysine, arginine, and ornithine) by the renal epithelial cells.

SIGNS AND SYMPTOMS

- Most common presenting symptom is abdominal/flank pain radiating to the genitalia (renal colic).
- Microscopic or gross hematuria.
- Dysuria and urgency, sometimes with concurrent UTI.
- Particularly in younger children, can be asymptomatic and diagnosed incidentally on abdominal imaging.

DIAGNOSIS

- Three imaging modalities used for diagnosis—noncontrast helical abdominal CT, ultrasound, and plain abdominal radiography.
  - Plain abdominal x-ray will show radiopaque stones (calcium, struvite, and cystine) but could miss small stones or those overlying bony structures.

WARD TIP

Urinary metabolic abnormalities are often the cause of pediatric stones:
- Hypercalciuria (most common)
- Hyperoxaluria
- Hypocitraturia

WARD TIP

Uric acid stones are radiolucent and thus cannot be seen on x-ray.

- Abdominal CT is the most sensitive modality and can help detect ureteral stones, radiolucent stones, and small stones which may be missed on x-ray. It will also show any structural anomalies or presence of hydronephrosis.
- Ultrasound is effective and avoids radiation; thus it should be used in pregnant females. Limited in ability to detect small stones, papillary, or ureteral stones. Can identify hydronephrosis that may help guide next steps.

TREATMENT

- Acute treatment:
  - Pain management: NSAIDs are mainstay; opiates may be needed.
  - Aggressive IV hydration.
  - Should obtain urine culture given high rate of concurrent UTI.
  - Majority of stones <5 mm will pass spontaneously.
  - Should undergo intervention to remove calculi if they are >5 mm, if signs of infection, obstruction, or renal insufficiency are present, or if stone doesn't pass.
  - Options for intervention include extracorporeal shock wave lithotripsy, percutaneous nephrostolithotomy, and ureteroscopy.
- Prevention of recurrence depends on metabolic abnormality.

Urinary Tract Infection (UTI)

👤 A 3-week-old infant presents with fever, vomiting, and decreased fluid intake. A UA reveals 100 WBCs. *Think: E. coli* UTI. *Next step: urine culture.*
Infants have nonspecific UTI symptoms, such as irritability, fever, and vomiting. *E. coli* is the most common organism in children of all ages. UA may show positive urinary leukocyte esterase, positive urinary nitrite, pyuria (>5 WBC/hpf), and bacteriuria.

👤 A 7-year-old girl presents with urinary urgency, frequency, suprapubic pain, and no flank pain or mass. UA shows many leukocytes, 2–5 RBCs, and no protein or casts. *Next step: urine culture.*
Older children have more localized UTI symptoms such as frequency, dysuria, and abdominal pain. The definitive diagnosis requires a positive urine culture from a specimen obtained with sterile techniques.

👤 A 6-month-old infant presents to the ER and is found to have a UTI. He is hospitalized and given IV antibiotics, but remains febrile. *Think: Pyelonephritis secondary to anatomic abnormality. Next step: Ultrasound.*
In infants, all UTIs are presumed to involve the kidneys and therefore should be treated with IV antibiotics. If infants remain febrile or UTI recurs, that may indicate an underlying anatomic abnormality or vesicoureteral reflux, so an ultrasound should be done.

DEFINITION

- Infection of the urinary tract by bacterial pathogens.
- UTIs are typically caused by fecal or genital bacteria. The most common is *E. coli* (85%), followed by *Klebsiella*, *Proteus*, and enteroccci. *Staphylococcus saprophyticus* is seen among female adolescents.

- UTIs are more common in males in the first year of life and in females afterwards.
- UTI occurs in 3–8% of girls and 1–2% of boys.

PREDISPOSING FACTORS

- Female sex.
- Uncircumcised male.
- Vesicoureteral reflux.
- Anatomic abnormalities.
- Bowel and bladder dysfunction (incontinence, holding urine, and eliminating with abnormal frequency or urgency).
- Sexual activity.
- Neurogenic bladder.

CLASSIFICATION OF UTIs

- **Pyelonephritis:** Infection of the kidney characterized by abdominal or flank pain, fever, malaise, nausea, vomiting, and diarrhea.
- **Cystitis:** Infection of the bladder. Common symptoms include dysuria, urgency, frequency, suprapubic pain, incontinence, and malodorous urine. Cystitis does not typically cause fever.
- **Asymptomatic bacteriuria:** Presence of >50,000/mL of a single bacterial organism on two successive urine cultures in a patient without any UTI-like symptoms or pyuria. No treatment is needed unless pregnant.

SIGNS AND SYMPTOMS

Symptoms vary with age:
- Neonates: Fever, failure to thrive, vomiting, jaundice. All febrile neonates should be evaluated for UTI.
- 2 months–2 years: Fever, poor feeding, vomiting, strong smelling urine, abdominal pain, irritability. Fever without a source may be evaluated for UTI based on clinical judgment.
- >2 years: Urinary urgency and frequency, bed-wetting, dysuria, strong smelling urine, abdominal or flank pain.
- Complications include renal scarring (loss of renal parenchyma), hypertension, and end-stage renal disease. Complications are more common with pyelonephritis, recurrent UTIs, and vesicoureteral reflux.

DIAGNOSIS

- Gold standard: Urine culture PLUS urinalysis. If child is not toilet trained, cultures must be obtained via suprapubic tap or catheterization.
- Diagnostic criteria: Pyuria (WBC >5/hpf) and/or positive Gram stain on UA and presence of >50,000 colonies in the urine culture. In asymptomatic children, pyuria must be present for diagnosis.
  - Urine nitrite is not sensitive in children, who empty their bladders frequently. The conversion of nitrates to nitrites by bacteria requires approximately 4 hours in the bladder. It is highly specific when present.
  - Leukocyte esterase is positive.
  - +/− Hematuria, white cell casts.

TREATMENT

Treatment varies depending on the age of the child:
- It is difficult to differentiate cystitis from pyelonephritis in children <2 years old, so treat the same initially.
- <2 months: 10–14 days of IV antibiotics. Start broad and narrow based on cultures. Usual choice is cephalosporin (cefotaxime). Gentamycin is added if <7 days old.

- >2 months: 7–14 days of oral or IV antibiotics based on local sensitivities. Usual choices include cephalosporins, amoxicillin-clavulanate, or trimethoprim-sulfamethoxazole.
- Avoid nitrofurantoin if <2 years due to high urinary voiding as it is excreted in the urine. It may be used for *S. saprophyticus* in adolescents.
- Bladder and renal ultrasounds can identify factors predisposing to UTIs including hydronephrosis, dilation or duplication of distal ureters, solitary kidney, echogenic stones, and perinephric abscess. Indications for ultrasound:
  - Children with two or more febrile UTIs.
  - Children <2 years old with one febrile UTI.
  - Children with nonfebrile UTI and risk factors (poor growth, hypertension, or a family history of urologic/renal disease).
  - Children who do not respond to antibiotics.
- A voiding cystourethrogram (VCUG) is used to diagnose vesicoureteral reflux, in which urine flows backwards from the bladder toward the kidneys during urination. To perform a VCUG, the bladder is filled with contrast via a catheter and images are taken during urination. Perform VCUG in:
  - Children with two or more febrile UTIs.
  - Children with one febrile UTI and an abnormal ultrasound or clinical risk factors.
- Renal cortical scintigraphy with DMSA determines acute functioning of the renal cortex and chronic renal scarring. It is done following an ultrasound that suggests renal damage. Radiotracer is injected into a vein and excreted by the kidneys.

INDICATIONS FOR INPATIENT TREATMENT

- Child cannot tolerate oral antibiotics.
- Toxic appearing.
- Pyelonephritis.

Vesicoureteral Reflux (VUR)

DEFINITION

- Retrograde flow of urine from the bladder to the ureter and renal pelvis.
- Reflux predisposes to pyelonephritis by facilitating the transport of bacteria from the bladder to the upper urinary tract.
- The most common cause of VUR is inadequate closure at the ureterovesicular junction, which commonly resolves spontaneously with growth.
- VUR may also be caused by abnormally high bladder pressures seen with posterior urethral valves and neurogenic bladder.

EPIDEMIOLOGY

- 30–45% of children with UTIs have reflux.
- More common in females.
- More common in children <2 years old.

DIAGNOSIS

- Most reflux is diagnosed by voiding cystourethrogram (VCUG) during a workup for a UTI.
- Prenatal ultrasonography showing hydronephrosis should receive a postnatal ultrasound with or without VCUG to determine if VUR is present.

GRADING

Reflux is graded on a scale of 1 (most mild) to 5 (most severe) depending on the extent of dilation of the ureter and kidney findings on VCUG.

TREATMENT

- The goal of treatment is to prevent pyelonephritis and renal injury.
- Treatment options include watchful waiting, antibiotic prophylaxis (sterile urine does not damage the kidney), and surgical correction.
- DMSA scans are performed to determine renal function (described in UTI section).
- Medical and surgical management is more appropriate with higher grade reflux and reflux beyond age 2–3. Surgical management is indicated for UTIs not responsive to antibiotics.

Neurogenic Bladder

DEFINITION

Abnormal innervation to the bladder and sphincter muscles, associated with spinal abnormalities such as spina bifida.

SIGNS AND SYMPTOMS

- Urinary incontinence.
- Urinary retention.
- Urinary tract infections (UTIs).
- Impaired renal function caused by hydronephrosis secondary to reflux.

TREATMENT

- Intermittent catheterization.
- Several surgical procedures exist to help prevent renal complications, promote continence, and facilitate self-catheterization.

Outflow Tract Obstruction

DEFINITION

- A range of anomalies resulting in a physical barrier between the uterus and vaginal introitus:
  - Imperforate hymen and incomplete hymenal fenestration.
  - Transverse or longitudinal vaginal septum.
  - Vaginal agenesis ("müllerian aplasia," Mayer-Rokitanski-Kuster-Hauser syndrome) is the absence of the upper vagina +/− uterus due to underdevelopment of the müllerian system. Associated with congenital anomalies (i.e., renal agenesis, horseshoe kidneys). External exam is normal due to separate development of urogenital sinus.

SIGNS AND SYMPTOMS

- Imperforate hymen and transverse vaginal membrane are total obstructions that can present in infancy as bulging from maternal estrogen withdrawal secretions. If not identified, mucus is reabsorbed and the anomaly presents in adolescence with cyclical abdominal pain, primary amenorrhea, bulging of the introitus, +/− a bluish membrane.
- Incomplete hymenal fenestration and longitudinal vaginal septa are incomplete obstructions that can be asymptomatic, cause dyspareunia or pain with insertion of tampons, or cause retained blood leading to spotting, malodorous discharge, or infection.
- Vaginal agenesis is the most common obstructive cause of primary amenorrhea, often detected in adolescence.

DIAGNOSIS

Diagnosis is clinical or made via ultrasound.

TREATMENT

Surgery. If asymptomatic, longitudinal septa does not require intervention. Dilators may be used for vaginal agenesis.

Polycystic Ovarian Syndrome (PCOS)

DEFINITION

- PCOS is the most commonly diagnosed ovarian cause of infertility and anovulation.
- Consider PCOS in female adolescents with the following primary complaints:
    - Hirsutism (excessive male-pattern hair growth on face, back, or chest).
    - Treatment-resistant inflammatory acne.
    - Menstrual irregularities.
    - Obesity accompanied by menstrual irregularities.

PATHOPHYSIOLOGY

- Excess androgen production by the ovaries.
- Linked to insulin resistance and obesity, but ~1/2 of women with PCOS are not obese.

SIGNS AND SYMPTOMS

- Hirsutism, acne, alopecia, menstrual abnormalities, infertility, obesity.
- Insulin resistance: Acanthosis nigricans, metabolic syndrome (increased risk for type 2 diabetes and cardiovascular disease), fatty liver disease.
- PCOS is a risk factor for endometrial hyperplasia and carcinoma.

DIAGNOSIS

- Clinical diagnosis if there is 1–2 years of abnormal uterine bleeding and evidence of hyperandrogenism.
- Abnormal uterine bleeding includes the following:
    - Primary amenorrhea: No menarche by age 15 or by 3 years after breast development.
    - Secondary amenorrhea: No menses for over 90 days after menarche.
    - Oligomenorrhea: <4 periods in the first year, <6 in year 2, <8 in year 3–5, <9 in year 6+.
    - Excessive uterine bleeding: More often than every 21 days (or 19 days in year 1), lasting over 7 days, or soaking through a pad or tampon every 1–2 hours.
- Evidence of hyperandrogenism includes high testosterone (best test) or moderate to severe hirsutism (clinically).
- Ultrasound is **not recommended** for diagnosis due to poor specificity in adolescent, but it can be used to rule out adrenal and ovarian tumors.
- Note that adolescent females often have irregular menses during the first few years after menarche. Make sure they fit the criteria for abnormal uterine bleeding!
- Other causes of hyperandrogenism to rule out include congenital adrenal hyperplasia, adrenal tumors, cortisone reductase deficiency, Cushing syndrome, thyroid dysfunction.

Treatment

- Combined estrogen/progestin oral contraceptive pills regulate menses, decrease androgen production, and reduce endometrial hyperplasia.
- Alternatives: Progestin-only contraception, gonadotropin-releasing hormone agonists.
- For hirsutism: Hair reduction (creams, laser therapy), antiandrogens (spironolactone).
- Lifestyle modification, glucose monitoring, +/– metformin for insulin resistance.

Ovarian Torsion

Definition

Twisting of the ovary on its vascular pedicle. Ovarian torsion is an **obstetrical emergency.**

Epidemiology

- Most common in women of reproductive age, but can occur in all ages.
- The biggest risk factors are large (>5 cm) ovarian masses, including cysts and neoplasms.
- Risk factors include pregnancy and ovulation induction.

Signs and Symptoms

- Acute sharp lower abdominal pain with nausea and vomiting.
- Pain may be unilateral or diffuse. In children pre-menses, it is more often diffuse leading to delays in diagnosis.
- An adnexal mass may be palpated.

Diagnosis

- Definitive diagnosis can only be made intraoperatively by direct visualization.
- A presumptive diagnosis is made clinically and on Doppler ultrasound showing decreased or absent blood flow, fluid around the ovary, and a change in gonadal location or size.

Treatment

- Surgical detorsion. Keep the ovary if possible, and remove any cyst (cystectomy) if found.
- If ovary is not viable, oophorectomy should be performed.
- Torsion is a surgical emergency. The longer it is torsed, the lower the chance of saving it.

Testicular Torsion

A 15-year-old boy presents with sudden onset of severe pain in his right testicle. A physical exam reveals a tender, swollen, firm testicle with a transverse lie. There is no cremasteric reflex on the right. *Think: Testicular torsion.*

Testicular torsion presents with nausea, vomiting, and severe acute testicular pain. Diagnosis is made clinically and surgical exploration should occur immediately in cases of high clinical suspicion.

DEFINITION

- Twisting of the testicle on its vascular pedicle.
- Most often due to poor fixation of the testis to the tunica vaginalis inside the scrotum.

EPIDEMIOLOGY

- Most common in boys 12–18 years. It also occurs in utero and in neonates.
- Undescended testes are a significant risk factor.

SIGNS AND SYMPTOMS

- Acute pain, erythema, and swelling of the scrotum.
- Nausea and vomiting.
- Absent **cremasteric reflex** (testicular elevation provoked by stroking the inner thigh).
- Testicle elevated or lies horizontally (**bell clapper deformity**).

DIAGNOSIS

- Definitive diagnosis can only be made by direct visualization in surgery.
- A presumptive diagnosis is made clinically and Doppler ultrasound shows decreased or absent blood flow, perigonadal fluid, and a change in gonadal location or size.

TREATMENT

- Torsion is a surgical emergency. "Time is testes."
- Surgical detorsion followed by fixation in scrotum (orchiopexy) or removal of the testicle (orchiectomy) if tissue is already dead.
- The contralateral testes is also explored and orchiopexy may be performed.

Phimosis/Paraphimosis

DEFINITION

- Phimosis: Inability to retract the prepuce (foreskin) over the glans penis. In newborns and younger children, phimosis is normal. In older males, it is pathologic (from scarring).
- Paraphimosis: Inability to return the prepuce over the glans from a retracted position. Leaving the prepuce retracted may cause venous and lymphatic congestion, followed by arterial compromise and penile infarction, which is a urologic emergency.
- Risk factors for paraphimosis:
    - Phimosis.
    - Recurrent infections.
    - Failure to return the foreskin over the glans after urologic procedures.
    - Forceful retraction of the foreskin resulting in scarring.
    - Penile piercing.

SIGNS AND SYMPTOMS

- Phimosis predisposes to urinary retention, UTIs, and inflammation of glans and prepuce.
- Epithelial cells may get trapped under phimotic foreskin and form benign cysts. Cysts help the phimotic foreskin to retract and resolve.
- Phimotic foreskin may balloon out with urination, which is benign unless urine is retained.
- Paraphimosis may present with swelling and tenderness of the penis and a band of circumferential tissue.

WARD TIP

Do not force retraction of the foreskin in phimosis. This may lead to paraphimosis. Return the foreskin over the glans after cleaning and sexual acts.

TREATMENT

- Phimosis: Reassurance and hygiene education. Most resolve spontaneously. Topical steroids and manual stretching loosen the phimotic ring. Circumcision may be offered.
- Paraphimosis: Pain control, reduce local swelling, and manually return the foreskin over the glans. In few cases where color change is present, urology consult may be needed.

Hypospadias

DEFINITION

- Congenital anomaly resulting in ventral displacement of the male urethra.
- Urethra located between the glans and perineum.
- If hypospadias occurs with undescended testes, consider disorders of sexual development.
- If hypospadias occurs with other congenital anomalies, ultrasound the upper urinary tract for anomalies.

SIGNS AND SYMPTOMS

- "Two urethral openings," with the second blind ending crevice at normal urethral position.
- "Dorsal hooded prepuce" (foreskin remains open ventrally).
- Abnormal penile curvature.
- Difficulty controlling urine direction.
- Severe hypospadias may cause erectile dysfunction and infertility.

TREATMENT

- No intervention or surgical repair at 6–18 months depending on severity.
- Avoid circumcision. It is not safe in children with a dorsal hooded prepuce and the foreskin is used for the future hypospadias surgery.

WARD TIP

It is important to not circumcise children with hypospadias, as the foreskin is used in the repair.

Epispadias

- Dorsal opening of the urethra on the penile shaft.
- Associated with more serious congenital abnormalities such as bladder exstrophy (inside out bladder that is exposed to the environment due to abnormal abdominal wall development), and/or cloacal exstrophy (exstrophy of bladder and large intestine).

Cryptorchidism ("Hidden Testes")

A 16-year-old healthy boy has sudden onset of abdominal and scrotal pain. A physical examination shows severe tenderness in the right inguinal canal, and the right scrotum is empty. *Think: Testicular torsion of an undescended testicle.*

Most undescended testes are in or distal to the inguinal canal. Torsion should be considered with inguinal pain or swelling in a boy with an undescended testis. Fixation of undescended testes may help prevent torsion.

DEFINITION

- Testicle not in the scrotum by 4 months. It may be absent or undescended.
    - Testes may be absent if there was agenesis or intrauterine testicular torsion and necrosis ("vanishing testes syndrome").
    - True undescended testes were halted during their descent and are in the abdomen (least common), inguinal canal, or at the external ring (most common).
    - Retractile undescended testes are elevated and can be manually brought into correct position and remain there if held for 1 minute.
    - Acquired undescended testes start descending and then ascend.
    - Ectopic testes descend, then move to perineal, femoral, suprapubic, or contralateral scrotal areas.
- Prematurity is a risk factor. Present in 30% of premature males.

SIGNS AND SYMPTOMS

- Empty, under-formed, or poorly rugated scrotal sac or hemiscrotum.
- +/− Inguinal fullness, palpable testes at the external ring or in the inguinal canal.
- Absence of testes on the left side is more common. It may also be bilateral.
- Increased risk for subfertility, malignancy, hernias, torsion, testicular cancer, and trauma.

TREATMENT

- Most descend spontaneously by 3–4 months.
- If born with testes nonpalpable bilaterally or unilaterally with hypospadias: Work up for sexual development disorders.
- If testes are not palpated or thought to be atrophic, do exploratory surgery at 6–12 months.
- Orchiopexy at 6–12 months reduces risk of torsion and subfertility. Malignancy risk remains increased, but testes can be examined more easily.
- If retractile, watch and wait until nondescent or descent is confirmed at puberty.

WARD TIP

Orchiopexy does not reduce the risk of testicular malignancy in cryptorchidism, but the testes can be examined more easily.

Sexually Transmitted Infections (STIs)

A 16-year-old boy presents with lower left abdominal pain and left testicular pain for 2 weeks. Palpation of the testes is normal except for isolated tenderness of the epididymis. Cremasteric reflex is normal. *Think: Epididymitis.*

Patients with epididymitis experience gradual scrotal pain and tenderness is localized to the epididymis +/− pyuria. Congenital genitourinary anomalies may predispose to recurrent infection. It can be difficult to differentiate from torsion.

A 15-year-old female presents to the ED with a fever and lower abdominal pain for 1 day, dyspareunia (pain with sex), and vaginal discharge. She had unprotected sexual intercourse with a new male partner recently. Physical exam reveals adnexal tenderness, cervical motion tenderness, and a friable cervix. *Think: Pelvic inflammatory disease (PID).*

Acute PID should be suspected in young females with pelvic pain. Empiric antibiotic treatment is recommended in **all** sexually active women with lower abdominal pain and cervical motion, adnexal, or uterine tenderness. Elevated temperature, leukocytosis (WBC >100,000), and purulent discharge may help with diagnosis, but treatment should be initiated even without these findings.

👤 A 3-year-old girl presents with malodorous bloody vaginal discharge. *Think: Foreign body.*
Foreign bodies can cause vaginal discharge, possibly malodorous or with bleeding. The most common foreign body in children is toilet paper.

EPIDEMIOLOGY

- Sexually transmitted infections affect ~25% of adolescents.
- In infants and children, detection of an STI is an important clue to sexual abuse.

RISK FACTORS

- Unprotected sex with an infected partner or multiple partners.
- History of a sexually transmitted infection.
- Injection drug use.
- Anal sex.

SIGNS AND SYMPTOMS

STIs can cause diverse symptoms:
- **Urethritis**: Dysuria, pyuria, erythema, urethral discharge. *Think: Gonorrhea or chlamydia.*
- **Vulvovaginitis:** Pruritus, vaginal discharge, erythema, soreness, dysuria.
  - In children, vulvovaginitis is also caused by enteric or respiratory flora (i.e., group A *Streptococcus*), vaginal flora, irritants, trauma, lichen sclerosis, or yeast infections.
- **Epididymitis:** Acute or subacute pain and swelling of the epididymis, sometimes with scrotal swelling or a tender nodule. *Think: Chlamydia or gonorrhea.*
  - Also caused by UTIs (especially with urinary tract anomalies), viruses.
- **Anogenital warts.**
- **Genital ulcers:** *Think: Syphilis, herpes.*
  - In children, also think of systemic causes (e.g., Crohn's) and other syndromes.
  - **Lipschultz ulcers** ("virginal" or "apthous" ulcers): Large, painful necrotic ulcers with purulent base, raised edges, systemic symptoms (ages 10–15 years). Etiology may be viral.
  - With oral ulcers, arthritis, uveitis, *think: Behçet syndrome.*
  - With ulcers in oropharynx and conjunctivitis, *think: Stevens-Johnson syndrome and toxic epidermal necrolysis.*

COMPLICATIONS

- **Pelvic inflammatory disease (PID):** Infection of the upper female genital tract due to bacteria that ascended from the vagina.
- Includes **endometritis** and **salpingitis** (inflammation of the Fallopian tubes).
- Presents as lower abdominal pain, dyspareunia +/− fever.
- Cervical motion, adnexal, and uterine tenderness, purulent cervical discharge.
- Can progress to tubo-ovarian abscesses, peritonitis, and perihepatitis (**Fitz-Hugh–Curtis syndrome**).
- Long-term complications of PID include infertility (10–20%), ectopic pregnancy (up to 10%), and chronic pelvic pain (15–20%).

🖐 **WARD TIP**

Due to the high rate of concurrent gonorrhea and chlamydia infection, treatment for gonorrhea (ceftriaxone) should always be included with that for chlamydia (azithromycin or doxycycline) and vice versa.

🖐 **WARD TIP**

Testicular torsion would cause decreased flow on ultrasound, while epididymitis causes increased flow with ultrasound. Epididymitis also presents with fever and presents with more gradual pain localized to the epididymis.

🖐 **WARD TIP**

Congenital anomalies that can cause chronic discharge include polyps, skin tags, and tumors. Sarcoma botryoides (rhabdomyosarcoma) is a lower reproductive tract malignancy that peaks at ages 2–5.

🖐 **WARD TIP**

PainFUL ulcers:
Chancroid (*Hemophilus ducreyi*)
Herpes
PainLESS ulcers:
Lymphogranuloma venereum (LGV)
Chancre in primary syphilis

PATHOGENS AND DIAGNOSIS

Initial Steps:

- In most cases, the diagnosis is clinical.
- Always test for gonorrhea, chlamydia, HIV +/– syphilis.
- Culture all lesions.
- Microscopy and culture of vaginal discharge.
- Gram stain of urethral discharge in adolescent males.
- +/– UA and urine culture.
- Doppler ultrasound is not required for epididymitis, but would show increased flow.

DISEASE	PATHOGEN	SYMPTOMS	DIAGNOSIS	TREATMENT
Chlamydia	*Chlamydia trachomatis*	Asymptomatic, mucopurulent cervicitis, PID, urethritis, most common cause of epididymitis if sexually active. Can cause conjunctivitis in newborns born to infected mothers	Nucleic acid amplification test (NAAT) of urine or discharge	Ceftriaxone and azithromycin
Gonorrhea	*Neisseria gonorrhoeae*	Asymptomatic, urethritis, cervicitis, PID, epididymitis, greenish mucoid discharge. Can cause conjunctivitis in newborns born to infected mothers	NAAT. If unavailable, do microscopy (for men only, shows gram-intracellular diplococci) or culture endocervical or urethral specimens	Ceftriaxone and azithromycin
HPV	Human papillomavirus	**Condyloma acuminata** are large flesh-colored, pink, or brown papules that can coalesce into "cauliflower" plaques. In children, more HPV strains cause genital warts. Can progress to cervical cancer in adults	Typically clinical. 5% acetic acid can turn HPV infected warts white. Biopsy can be done if uncertain. Do not do cervical screenings until age 21	Watch and wait. Many regress on own. Multiple therapies available for condyloma acuminata, but recurrence is common
Herpes*	Herpes simplex virus	Multiple painful vesicles on an erythematous base (HSV1 and HSV2) +/– urethritis	Viral culture, PCR testing, direct fluorescence antibody, or serologic tests of lesion	Antiviral (e.g., acyclovir) and supportive care (sitz bath, topical creams)
Syphilis	*Treponema pallidum*	Primary syphilis: Painless chancre. If not treated, can present with systemic symptoms	Non-treponemal RPR or VDRL followed by treponemal FTA-ABS	Penicillin
Trichomoniasis	*Trichomonas vaginalis*	Urethritis, vulvovaginitis, yellow-green discharge	Microscopy with flagellated organisms is the first test for women. If negative or in men, do culture or NAAT	Metronidazole
Bacterial vaginosis**	Anaerobic bacteria (e.g., *Gardnerella vaginalis*)	White-gray vaginal discharge with fishy odor, vulvovaginitis	Clinical diagnosis +/– microscopy with +KOH "whiff test," visualization of **clue cells** (epithelial cells coated with bacteria), and pH >4.5	Metronidazole, male partners do not need treatment

Disease	Pathogen	Symptoms	Diagnosis	Treatment
Yeast infection**	*Candida albicans*	Itchy curd-like discharge with vulvovaginitis	Clinical diagnosis +/− visualization of budding yeast with a KOH stain	Topical azoles
HIV	Human immunodeficiency virus	Many systemic presentations	Immunoassay	Antiretroviral therapy

* May be caused by sexual contact OR auto-innoculation (herpetic whitlow, herpetic stomatitis).

** Non-STI causes of vaginal complaints.

SCREENING AND PREVENTION

- Give all children, regardless of gender, the HPV vaccine. Age recommendation is between 9–26 years for females and by 21 years for immunocompetent males.
- All females should receive Pap smear cytologic testing every 3 years to screen for cervical dysplasia starting at the age of 21. Women under 21 should not be screened for HPV, regardless of sexual history.
- Annually screen all sexually active adolescent females and high-risk males for chlamydia and gonorrhea (NAAT).
- HIV testing depends on risk factors and local practices. Typically screen ages 13+ at least once, and repeat annually if high-risk. Consider PREP (pre-exposure HIV prophylaxis) in high-risk patients (e.g., patients with HIV+ partners).
- Annually screen high-risk males for syphilis (nontreponemal RPR or VDRL followed by treponemal FTA-ABS).
- Patient education on safe sexual practices.
- If sexual abuse is suspected, social services and law enforcement agencies must be contacted. Forensic evidence should be collected within 24 hours (or ASAP), STI prophylaxis and testing may be done based on age and preferences. Emergency contraception should be highly encouraged for postpubertal females. Refer to mental health services.

TREATMENT

- Treat the underlying infection and test partners.
- For epididymitis, supplement with scrotal support, pain control, bed rest.
- If caused by respiratory or enteric flora, provide hygiene education.
- For PID, give 10–14 days of empiric broad-spectrum antibiotics (e.g., cefoxitin + doxycycline) with anaerobic coverage if there was recent instrumentation.
- For vaginal ulcers, give pain control. If severe, give topical corticosteroids.

NOTES

HIGH-YIELD FACTS IN

Hematologic Disease

TABLE 15-1. Normal Hemoglobin and Mean Corpuscular Volume (MCV) by Age

AGE	HGB (G/DL)	MCV (FL)
Birth	13.5–24.0	95–121
< 2 month	10.0–20.0	
2–6 months	9.5–14.0	
6 months–2 years	10.5–13.5	70–86
2–12 years	11.5–15.5	
12–18 years	12.0–16.0	78–102

Normal Hemoglobin by Age

Normal values of hemoglobin and red cell parameters vary with age, race, and gender (see Table 15-1).

Anemia

DEFINITION
Reduction in red blood cell (RBC) mass or blood hemoglobin concentration.

CLASSIFICATION
- RBC size and hemoglobin content (mean corpuscular volume [MCV], mean corpuscular hemoglobin concentration [MCHC]) (see Table 15-2).
- Mechanism—loss/sequestration, ↑ destruction, ↓ production.

PATHOPHYSIOLOGY
- Less oxygen transport.
- ↓ blood volume.
- ↑ cardiac output.

SIGNS AND SYMPTOMS
- Somnolence, light-headedness, headache.
- Angina, dyspnea, palpitations, flow murmur.
- Fatigue, claudication, edema.
- Pallor—conjunctiva, palmar creases.
- Hepatosplenomegaly in some cases.
- Irritability.
- Pica: Desire to eat unusual things (e.g., clay).

DIAGNOSIS
- Family history.
- Exposure history.
- Past medical history, including medications.
- Physical exam.

TABLE 15-2.   Anemias

MCV	MCHC	ANEMIA	RDW	SMEAR	LABS
Microcytic <80 (↓ Hgb production)	Hypochromic	Iron deficiency	↑	Elliptocytes Nucleated/Target RBCs	↓ ferritin, ↓ TIBC ↑ platelets
		Thalassemia	+/− NI		↑ Red cell count
		Lead toxicity		Stippled RBCs	
	Normochromic	Neoplastic			
Normocytic 80–100	Normochromic	Acute blood loss		Schistocytes	Bilirubin/LDH
		Hemolytic (microangiopathic)	NI		
		Anemia of chronic disease	NI		↓ TIBC
		Hemoglobinopathy	NI	Target cell	
		Renal disease		Acanthocyte	BUN/creatinine
Macrocytic >100 (defective DNA synthesis)	Normochromic	Hemolytic (autoimmune)	↑	Spherocytes	Bilirubin/LDH Direct Coombs' test
		Alcohol	NI	Round	
		Liver disease	NI	Round, target, echinocyte, acanthocyte	
		Aplastic anemia	NI		T$_4$/TSH
		Hypothyroidism	↑	Round	
		Drug effect (e.g., hydroxyurea)		Oval	
		Myelodysplasia		Oval, dacrocyte	
Megaloblastic >110 (defective DNA synthesis)		Folate deficiency	↑	Oval PMN segmented	↓ reticulocytes ↓ serum folate ↑ homocysteine
		B$_{12}$ deficiency/pernicious anemia	↑	Oval PMN segmented	↓ serum cobalamin Schilling test ↓ reticulocytes ↑ serum methylmalonic acid and homocysteine

BUN, blood urea nitrogen; LDH, lactic dehydrogenase; MCV, mean corpuscular volume; MCHC, mean corpuscular hemoglobin concentration; PMN, polymorphonuclear neutrophil; RBC, red blood cell; RDW, red cell distribution width; T$_4$, thyroxine; TIBC, total iron-binding capacity; TSH, thyroid-stimulating hormone.

- Complete blood count (CBC): See Table 15.2.
- Peripheral blood smear: See Table 15-3.
- Platelet and white blood cell (WBC) size, morphology.
- Possible bone marrow aspirate/biopsy—cellularity, morphology, stroma.
- Chemistry—liver function tests (LFTs), lactic dehydrogenase (LDH), creatinine (Cr), uric acid.
- Imaging as appropriate.
- Other special tests—serum ferritin, B$_{12}$, folate, reticulocyte count, Coombs' test, osmotic fragility, etc.

TABLE 15-3. Some Erythrocyte Morphology and Inclusion Bodies

CELL	SPHEROCYTE	TARGET CELL	ECHINOCYTE (BURR)	ACANTHOCYTE	DACROCYTE
Description	Round, no central clearing	Concentric circles	Evenly spaced projections (spikes)	Irregularly spaced projections	Teardrop shape
Mechanism	Defective RBC membrane	↑ in membrane to Hgb ratio	Spiculed, crenated	Excess lipid in membrane	Extramedullary hematopoiesis
Etiologies	Hereditary spherocytosis Autoimmune hemolytic anemia	Liver disease Hemoglobinopathies (e.g., Hgb C, S) Postsplenectomy Thalassemia	Liver disease Postsplenectomy Azotemia/uremia Gastric carcinoma	Liver disease Renal failure Splenic disease DIC Pyruvate kinase deficiency	Myelofibrosis

CELL	SCHISTOCYTE	SICKLE CELLS	BASOPHILIC STIPPLING	HOWELL-JOLLY BODY	HEINZ BODIES
Description	"Bite cell"	Pointed	Round, dark-blue granules in the cell	Densely blue cytoplasmic inclusions	Round protuberances deforming the cell
Mechanism	Mechanical damage		Aggregated ribosomes	Nuclear fragments	Oxidized/ denatured Hgb
Etiologies	G6PD deficiency DIC HUS Vasculitis	Sickle cell disease	Sideroblastic anemia Myelodysplastic syndrome Heavy metal poisoning	Hemolytic anemia Megaloblastic anemia Hyposplenism Postsplenectomy	Oxidative medications, chemicals Abnormal Hgb (H, Köln) Enzyme deficiencies (G6PD)

DIC, disseminated intravascular coagulation; G6PD, glucose-6-phosphate dehydrogenase; HUS, hemolytic-uremic syndrome; RBC, red blood cell.

TREATMENT

- Supplement or remove causative factor.
- Support hemodynamics as appropriate.

PHYSIOLOGIC ANEMIA OF INFANCY

- Normal newborns have higher hemoglobin until third week.
- ↓ to 9–11 g/dL at 8–12 weeks.
- Decline in hemoglobin level is both more extreme and more rapid in premature infants: 7–9 g/dL by 3–6 weeks.

ETIOLOGY

- Abrupt cessation of erythropoiesis with the onset of respiration.
- ↓ survival of fetal RBCs (60 days versus 120 days).
- Expansion of blood volume in first 3 months.
- No therapy needed.
- As hemoglobin approaches its nadir, erythropoietin is produced with subsequent resumption of erythropoiesis.

TRANSIENT ERYTHROBLASTOPENIA OF CHILDHOOD

A previously healthy 1-year-old male infant had a cold 8 weeks ago. He now is pale and irritable and refuses to eat. A CBC shows Hgb 5.0, Hct 10%, MCV 80, reticulocyte count 0%, WBC 9, platelets 400K. *Think: Transient erythroblastopenia of childhood (TEC).*
TEC occurs in previously healthy children and is often preceded by a viral infection. Classic history is gradual onset of pallor between the ages of 1 and 4 years. Characteristic features include normocytic anemia, severe reticulocytopenia, transient neutropenia, and ↑ platelet counts. It is often confused with Diamond-Blackfan anemia. TEC is a self-limited condition and has an excellent prognosis.

- Transient erythroblastopenia of childhood (TEC).
- The most common acquired red cell aplasia in children.
- Age 6 months to 5 years (most children >12 months).

Diamond-Blackfan should be differentiated from transient erythroblastopenia of childhood based on the features listed.
- Age (average age of diagnosis = 3 months).
- Macrocytic (↑ MCV).
- Reticulocytopenia.

DEFINITION

Transient failure of the bone marrow to produce RBCs usually at 18–26 months; may occur at <6 months and up to 5 years.

ETIOLOGY

Possible link to parvovirus B19.

SIGNS AND SYMPTOMS

Gradual pallor and fatigue; appearance better than expected for Hgb level.

DIFFERENTIAL DIAGNOSIS

- Diamond-Blackfan anemia.
- Etiology: Genetic.
- Age: During first year.
- ↑ MCV.
- ↑ Red cell adenosine deaminase (ADA).
- ↑ Hemoglobin F.
- ↑ i Antigen.

DIAGNOSIS

- CBC: Hgb 5–7, clinically insignificant neutropenia.
- Normochromic, normocytic anemia (MCV normal for age).
- Reticulocyte count initially <1%, ↑ with recovery (↑ MCV during recovery).
- Any child with presumed TEC who requires more than one transfusion should be considered for alternate diagnoses.

TREATMENT

- Supportive until RBC production returns; should occur spontaneously in 30–60 days.
- If continues, different causes of the anemia must be investigated.

WARD TIP

Normal newborn Hgb is 14–20 g/dL.

WARD TIP

Schilling test: Radiolabeled B_{12} used to investigate B_{12} deficiency.

Nutritional Anemias

IRON DEFICIENCY ANEMIA

A 9-month-old child who has been fed whole milk from early infancy presents with the following lab values: Hgb 7.5 g, MCV 62, RBC 3.2. *Think: Iron deficiency anemia.*

Consumption of large amounts of cow's milk is the most common dietary pattern in children with iron deficiency anemia. Cow's milk has poor iron bioavailability, especially in infants <12 months. In the first year, full-term infants need to absorb 1.2 mg of elemental iron. Since only up to 10% of dietary iron is absorbed, daily intake of iron should exceed 12 mg. Characteristic findings are microcytic, hypochromic anemia, low mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH), ↑ red cell distribution width (RDW), and ↓ reticulocyte count. Depletion of iron stores is the earliest finding.

ETIOLOGY

- Inadequate intake (whole cow's milk has no iron).
- Loss of iron.
- Bleeding.
- Rapid growth spurts (early infancy and adolescence).
- Prematurity (↓ iron stores).
- Chronic diseases (juvenile rheumatoid arthritis [JRA], cystic fibrosis [CF]).

EPIDEMIOLOGY

- Most common anemia in children.
- Especially 6 months to 3 years old.
- Rare in infants under 6 months.

SIGNS AND SYMPTOMS

- Usual symptoms of anemia (pallor, fatigue).
- Cheilosis/angular stomatitis, glossitis.
- Koilonychia (spoon nails).
- Esophageal web.
- Blue sclera.
- Splenomegaly.

DIAGNOSIS

- ↓ serum ferritin (<10 ng/mL).
- ↓ serum iron.
- ↑ iron-binding capacity.
- Microcytic and hypochromic, ↑ RDW.
- Low reticulocyte count.
- ↑ platelet count (>600,000/mm³).
- Hypercellular marrow with erythroid hyperplasia.
- ↓ stainable iron.

TREATMENT

- Ferrous sulfate 3–6 mg/kg/day for at least 8 weeks after a normal Hgb level is obtained.
- Retic response to oral iron within 4 days.

WARD TIP

Mentzer Index
MCV/RBC
≥13.5 Iron deficiency (also will see an increased RDW)
≤11.5 Thalassemia trait

WARD TIP

Remember: Ferritin is an acute phase reactant. A normal or high ferritin does not exclude iron deficiency during an acute infection.

LEAD POISONING

A 2½-year-old boy with hyperactivity lives in old apartment building with peeling paint on the walls. His gait has become ataxic and his speech has regressed. His Hgb is 8.5 g. *Think: Lead poisoning.*

Lead poisoning is usually caused by exposure to dust and paint chips from interior surfaces of homes. The initial signs and symptoms may be nonspecific. Laboratory screening should be considered for children at risk for lead poisoning and should be screened routinely starting at age 1 year. A blood lead level of ≥10 µg/dL is considered abnormal. To avoid contamination, a venous sample should be obtained for confirmation. Other features are anemia and basophilic stippling on peripheral smear and elevated free erythrocyte protoporphyrin level.

> **EXAM TIP**
>
> Chronic lead poisoning interferes with iron utilization and hemoglobin synthesis.

DEFINITION

Variant of iron deficiency anemia.

ETIOLOGY

- Environmental (aerosolized and oral); dust.
- Lead-containing paint.
- Associated with PICA.

PATHOPHYSIOLOGY

- Irreversible binding with sulfhydryl group of proteins.
- Inhibits enzymes involved in heme production.
- Impairs iron utilization.

> **EXAM TIP**
>
> Screening for lead poisoning occurs at 10–14 months and at 2 years of age.

SIGNS AND SYMPTOMS

- Acute (lead level >60):
  - Headache
  - Abdominal Pain
  - Loss of Appetite
  - Constipation
  - Acute encephalopathy. (levels >100)
- Lead lines—thick transverse radiodense lines in the metaphyses of growing bones on radiographs.
- Chronic:
  - Cognitive impairement (decreased IQ).
  - ADHD.

DIAGNOSIS

- Microcytic hypochromic anemia, basophilic stippling.
- ↑ serum lead and free erythrocyte protoporphyrin (FEP) level. Lead level <9 is considered acceptable.
- ↑ urine coproporphyrin.

> **WARD TIP**
>
> Although chelation therapy for children with lead level between 20 and 44 µg/dL can lower blood level concentrations, it does not diminish cognitive impairement or other behavioral or neuropsych effects of lead.

TREATMENT

- Environment control, education, level dependent.
- 70 µg/dL—medical emergency: Dimercaprol (BAL) followed by ethylene-diaminetetraacetic acid (EDTA)—5 days' treatment.
- 45–69 µg/dL: Both medical and environmental intervention including chelation (EDTA or DMSA).
- 20–45 µg/dL: Environmental evaluation positive.
- 10–19 µg/dL: Education.
- Prevention: Banning of lead-based paint in 1978.

> **WARD TIP**
>
> Lead paint remains the most common cause of lead poisoning.

FOLATE DEFICIENCY

DEFINITION

Megaloblastic anemia.

ETIOLOGY

- Rare in children.
- Deficient intake or absorption.
- Pregnancy ($\uparrow$ requirement).
- Very-low-birth-weight (VLBW) infants.
- Drugs (phenytoin, methotrexate).
- Vitamin C deficiency.
- Goat's milk formula fed.

EPIDEMIOLOGY

Peak age 4–7 months.

SIGNS AND SYMPTOMS

- Features of anemia.
- Failure to gain weight.
- Chronic diarrhea.

DIAGNOSIS

- Macrocytic anemia, thrombocytopenia, neutropenia (hypersegmented PMNs).
- Low reticulocyte count.
- $\uparrow$ LDH.
- Bone marrow hypercellular and megaloblastic changes.
- Serum and RBC folate levels.

TREATMENT

- Parenteral folic acid only after confirmation.
- Folic acid is contraindicated in vitamin B_{12} deficiency, because it will mask anemia, yet B_{12} deficiency neurologic symptoms will progress.

VITAMIN B₁₂ DEFICIENCY

DEFINITION

Megaloblastic anemia.

ETIOLOGY

- Inadequate intake (strict vegetarians).
- Pernicious anemia.
- Surgery of stomach or terminal ileum.

PATHOPHYSIOLOGY

Deficiency of intrinsic factor due to autoimmunity or gastric mucosal atrophy prevents adequate B_{12} absorption.

SIGNS AND SYMPTOMS

- Juvenile pernicious anemia.
- Red, beefy tongue.

- Premature graying, blue eyes, vitiligo.
- Myxedema, gastric atrophy.
- Weakness, irritability, anorexia.
- Neurologic (ataxia, paresthesias, hyporeflexia, Babinski response, clonus).

DIAGNOSIS

- Macrocytic anemia, large hypersegmented neutrophils.
- ↑ LDH.
- Methylmalonic acid in urine.
- Anti-intrinsic factor antibody.
- Schilling test.

TREATMENT

- Vitamin B_{12} IM monthly.
- Oral therapy is contraindicated.

COPPER DEFICIENCY

PATHOPHYSIOLOGY

Copper is essential for production of red blood cells, transferrin, and hemoglobin.

SIGNS AND SYMPTOMS

- Refractory anemia, pancytopenia.
- Osteoporosis.
- Ataxia, spasticity.
- Menke disease in newborns—X-linked.

ETIOLOGY

- Copper-deficient total parenteral nutrition (TPN).
- Persistent infantile diarrhea.
- Post-gastric bypass surgery.
- Zinc supplementation (↓ copper absorption).

DIAGNOSIS

- Hypochromic anemia unresponsive to iron supplementation.
- Neutropenia.
- Impaired bone calcification.
- Serum copper and ceruloplasmin levels.

TREATMENT

Treat underlying cause.

ANEMIA OF CHRONIC DISEASE

ETIOLOGY

- JRA, systemic lupus erythematosus (SLE), ulcerative colitis.
- Malignancies.
- Renal disease.

DIAGNOSIS

- Can be normochromic and normocytic or hypochromic and microcytic.
- Hgb ranges 7–10 g/dL.

- Low serum iron with normal or low total iron-binding capacity (TIBC).
- Elevated serum ferritin.

TREATMENT

- Treat underlying cause.
- Iron if concomitant iron deficiency is present.

Hemolytic Anemias

See Figure 15-1.

Mediated either by intrinsic disorders of the red cell or by disorders extrinsic to the red cell itself.

SIGNS AND SYMPTOMS

- Can vary from asymptomatic to generalized symptoms to severe pain crises.
- Icterus, fever, splenomegaly.
- ↑ products of RBC destruction.
- Compensatory ↑ in hematopoiesis-reticulocytosis.
- See Table 15-4.

DIAGNOSIS

- ↑ direct bilirubin.
- ↓ haptoglobin (intravascular especially).
- ↑ hemoglobinuria/hemosiderinuria (intravascular).
- ↑ LDH.

```
                        ┌──────────┐
                        │ Hemolysis │
                        └──────────┘
            ┌───────────────┴────────────────┐
      ┌─────────┐                      ┌──────────┐
      │ Immune  │                      │ Nonimmune│
      └─────────┘                      └──────────┘
          │                      ┌──────────┴──────────┐
  • Hemolytic                ┌─────────┐          ┌──────────┐
    transfusion              │Intrinsic│          │Extrinsic │
    reaction (acute or       └─────────┘          └──────────┘
    delayed
  • Hemolytic disease
    of the newborn
    (Rh
    incompatibility)
  • Autoimmune
    hemolytic anemia
    • Idiopathic
    • Lymphoproliferative
    • Drugs
    • Connective
      tissue disease
```

Intrinsic branches:
- Enzyme defect
  - • G6PD
  - • Pyruvate kinase deficiency
  - • Hexokinase deficiency
- Membrane defect
  - • Hereditary spherocytosis
  - • Elliptocytosis
  - • Pyropoikilocytosis
- Hemoglobin defect
  - • Sickle cell anemia
  - • Thalassemia

Extrinsic:
- • Microangiopathic hemolytic anemia
  - • Heart valve
  - • TTP/HUS
  - • DIC
- • Infections
  - • Babesiosis
  - • Malaria
- • Chemicals
- • Venoms
- • Thermal injury
- • Hypophosphatemia

FIGURE 15-1. **Hemolytic anemias.**

TABLE 15-4.   **Hemolysis**

FEATURE	EXTRAVASCULAR	INTRAVASCULAR
RBC morphology	Abnormal	Normal
Hemoglobinemia/uria	–	+
Hemosiderinuria	–	+
Serum haptoglobin	Normal	↓
Splenomegaly	+	–
Examples		Transfusion reactions
		Microangiopathic hemolytic
		Infections: babesiosis, malaria
		G6PD deficiency
		Paroxysmal nocturnal hemoglobinuria

G6PD, glucose-6-phosphate dehydrogenase; RBC, red blood cell.

HEMOLYTIC DISEASE OF THE NEWBORN

DEFINITION

Erythroblastosis fetalis.

ETIOLOGY

Destruction of red blood cells of the neonate or fetus by maternal immuno-globulin G antibodies to RH, ABO, or other blood system antigens (kelly, Duffy).

PATHOPHYSIOLOGY

- Paternal heterozygosity allows an Rh-positive (or other alloantibody) infant to be carried by an Rh-negative mother.
- Maternal blood comes into contact with fetal blood cells.
- Maternal antibodies are produced against the Rh antigen.
- During a subsequent pregnancy with an Rh-positive infant, maternal antibodies cross the placenta and bind to fetal RBCs, → hemolysis.
- Destruction of RBCs causes ↑ unconjugated bilirubin, becoming clinically apparent only after delivery as the placenta effectively metabolizes it.
- Severe anemia → ↑ extramedullary erythropoiesis, with potential replacement of hepatic parenchyma.

EPIDEMIOLOGY

- Severe Rh disease is rare in the United States nowadays.
- Rh sensitization occurs in 11 of 10,000 pregnancies.
- <1% of births are associated with significant hemolysis.
- Approximately 50% of affected newborns do not require treatment, 25% are term but die or develop kernicterus, and 25% become hydropic in utero.

SIGNS AND SYMPTOMS

- Range from mild, self-limited, hemolytic disease to severe life-threatening anemia (hydrops fetalist).
- Hemolytic anemia.
- Fetal hydrops:
    - Large placenta.
    - ↑ unconjugated hyperbilirubinemia—rapidly progressive jaundice after birth, kernicterus.
    - Abdominal distention—hepatosplenomegaly, ascites, hepatic dysfunction.
    - Abduction of limbs, loss of flexion.
    - Scalp or skin edema.
    - Pleural or pericardial effusion.
    - Purpura.
    - Cyanosis.

DIAGNOSIS

Positive direct Coombs' test.

Reticulocytosis

TREATMENT

- Know blood types of both parents early in the pregnancy.
- Prophylaxis (RhoGam) during and immediately after delivery for mothers at risk for alloimmunization.
- Exchange transfusion to infant of Rh-negative blood.

SICKLE CELL DISEASE (SCD)

A 16-month-old African-American boy is brought to the ED because of crying and refuses to stand. He has no fever, vomiting, or diarrhea. His parents denied trauma or fall. On examination, he is afebrile. He cries when his right leg is touched. X-ray of his right leg showed no fracture. *Think: Sickle cell disease.*

Acute sickle cell painful episode (painful crisis) is the most common presentation in children with SCD. Newborn screening has resulted in detection in early infancy. CBC shows chronic hemolytic anemia with low hematocrit and hemoglobin levels and a reticulocytosis. Peripheral smear may show sickled forms, target cells, and polychromasia suggestive of reticulocytosis.

DEFINITION

Chronic hemolytic anemia due to premature destruction of red cells.

ETIOLOGY

Defect in β-globin–hemoglobin S (HgbS)—substitution of glutamic acid at sixth position of β-chain by valine.

PATHOPHYSIOLOGY

- Unusual solubility problem in the deoxygenated state.
- HgbS is a low-affinity hemoglobin.

EPIDEMIOLOGY

- Autosomal recessive.
- One in 500 African-Americans.
- Eight percent of African-Americans are carriers.

SIGNS AND SYMPTOMS

- Appears after 6 months of age (when HbF is ↓).
- Anemia (due to hemolysis).
- Vaso-occlusive: Leg ulcers, stroke, priapism, pain crises.
- Hand-foot syndrome (swollen hands and feet).
- Infection (encapsulated organisms):
    - *Streptococcus pneumoniae* (30%).
    - *Haemophilus influenzae.*
    - *Salmonella* osteomyelitis.
- Splenomegaly—initially, but splenic infarction leads to functional asplenia.
- Cardiac enlargement; myocardial infarction.
- Short stature, delayed puberty.
- Gallstones/jaundice.
- Renal infarction.

DIAGNOSIS

- Newborn screening.
- Hgb electrophoresis (definitive test).
- HgbS 90%.
- HgbF 2–10%.
- No HgbA.
- Hgb ranges 5–9 g/dL.
- Peripheral smear—target cells and sickled cells.
- ↑ WBCs and platelets.

TREATMENT

- Infection prevention:
    - Pneumococcal conjugate vaccine (PCV13)—4 doses before 23 months.
    - Pneumococcal vaccine (23 valent) (at 2 and 5 years).
    - Menigococcus (can be given after 2 years old).
- Prophylactic penicillin by 4 months of age (until 5 years old).
- Painful crisis—hydration and analgesics.
- Priapism—exchange transfusion.
    - Hydroxyurea—reduces incidence of acute painful episodes and hospitalization rates.

> **EXAM TIP**
>
> The most common cause of fatal sepsis in patients with sickle cell disease is *Streptococcus pneumoniae.*

> **WARD TIP**
>
> There now exists universal newborn screening for sickle cell disease.

> **WARD TIP**
>
> Fever in SCD should be considered a medical emergency.

> **EXAM TIP**
>
> Hydroxyurea is the mainstay of overall treatment and prolonged survival.

THALASSEMIA

> A 2-year-old boy has required transfusion since early infancy. *Think:* β-*Thalassemia major.*
>
> Children with β-thalassemia usually become symptomatic in early infancy because of progressive hemolytic anemia and cardiac decompensation. Severe hypochromia and microcytosis is the characteristic of β-thalassemia. The hemoglobin level declines progressively in the first year and may be as low as 3–4 g/dL, requiring transfusion.

DEFINITION

Hereditary hemolytic anemia.

ETIOLOGY

Total or partial deletions of globin chain:
- **α-Thalassemia (gene deletion):**
    - Hgb Bart's (four-gene deletion).
    - HgbH (three-gene deletion).

- α-Thalassemia minor (two-gene deletion).
  - Silent carrier (one-gene deletion).
- **β-Thalassemia:**
  - Homozygous (β-thalassemia major).
  - Heterozygous (β-thalassemia minor).

SIGNS AND SYMPTOMS

- Severe hemolytic anemia.
- Hepatosplenomegaly.
- Extramedullary hematopoiesis (classic facies—maxillary overgrowth and skull bossing).

DIAGNOSIS

- Hypochromic, microcytic anemia.
- Hgb <5 g/dL.
- Reticulocytopenia.
- Markedly ↑ LDH (ineffective erythropoiesis).
- Hgb electrophoresis:
  - HgbA: ↓ or absent.
  - ↑ HgbA$_2$.
  - HgbF: Marked elevation.

TREATMENT

- Monthly transfusion of packed RBCs to maintain Hgb >10 g/dL.
- Splenectomy if requiring >240 mL/kg of packed RBCs/year.

Hemolytic Enzymopathies

GLUCOSE-6-PHOSPHATE DEHYDROGENASE (G6PD) DEFICIENCY

A previously well 2-year-old African-American male child is treated with sulfonamide. Two days later, he develops fever, back pain, dark urine, and anemia. Blood smear shows fragmented erythrocytes. *Think: G6PD deficiency.*

The highest prevalence of G6PD deficiency is in Africans and people of Mediterranean descent. It is a recessive X-linked trait; therefore, males are at higher risk. Episodic hemolysis is the characteristic of G6PD deficiency. It is caused by exposures that cause oxidant stress such as infection or drugs. Sulfonamides and antimalarial drugs (primaquine and chloroquine) are the common agents.

A male child has sudden onset of dark urine, pallor, and jaundice after an exposure to an oxidant stress. *Think: G6PD deficiency.*

Most patients are asymptomatic unless exposed to an oxidant stress that results in a hemolytic crisis. Jaundice and splenomegaly may be present during an acute crisis. Heinz bodies, indicative of denatured hemoglobin, are typically present and can be detected by a methyl violet stain. G6PD levels can be deceptively normal during an acute crisis because of an elevated reticulocyte count. Therefore, G6PD levels should be obtained weeks to months later to obtain an actual baseline measurement.

DEFINITION

- Enzyme defect of hexose monophosphate (HMP) pathway, resulting in hemolysis when exposed to stresses such as infection or certain drugs.
- Develops 24–48 hours after the exposure of an oxidizing agent.

ETIOLOGY

Hereditary ↓ of G6PD that normally maintains adequate level of glutathione in a reduced state in RBCs.

PATHOPHYSIOLOGY

- Oxidized glutathione complexes with Hgb, forming Heinz bodies.
- RBC less deformable.
- Splenic macrophages "bite out" RBCs.

EPIDEMIOLOGY

- Most common hemolytic enzymopathy.
- X-linked.
- Higher incidence in African-American, Middle Eastern, and Mediterranean populations.

SIGNS AND SYMPTOMS

- Episodic intravascular hemolysis secondary to oxidant stress (drugs, fava beans, etc.).
- Spontaneous chronic nonspherocytic hemolytic anemia.
- Jaundice, dark urine.
- Splenomegaly.
- Tiredness, headache.

DIAGNOSIS

- Reduced G6PD activity in RBCs.
- Anemia, Heinz bodies, and bite cells on peripheral smear.
- Reticulocytosis.
- Elevated serum bilirubin and LDH.
- ↓ serum haptoglobin.
- Hemoglobinuria.

TREATMENT

- Removal of oxidant stressor.
- Avoidance of known triggers.
- Oxygen.
- Transfusion of packed RBC for Hgb <6, hemodynamic instability, ongoing hemolysis.

PYRUVATE KINASE (PK) DEFICIENCY

DEFINITION

Congenital hemolytic anemia (↓ RBC PK).

PATHOPHYSIOLOGY

Pyruvate kinase catalyzes the final step in the glycolytic pathway.

EPIDEMIOLOGY

- Second most common hemolytic enzymopathy.
- Autosomal recessive.

SIGNS AND SYMPTOMS

- Chronic hemolytic anemia.
- Hyperbilirubinemia/failure to thrive (FTT) in newborn.

> **WARD TIP**
>
> Suspect G6PD deficiency when G6PD activity is within low normal range in the presence of high reticulocyte count.

> **EXAM TIP**
>
> G6PD deficiency protects against parasitism of erythrocytes (such as malaria).

> **WARD TIP**
>
> Drugs causing hemolysis in G6PD deficiency:
> - Aspirin
> - Sulfonamides
> - Ciprofloxacin
> - Antimalarials

> **WARD TIP**
>
> PK activity measured in erythrocytes is reduced markedly, but enzyme activity in other blood cells and tissues are normal.

- ↓ reticulocytes (selective destruction).
- Severity of hemolysis is variable.

DIAGNOSIS

↓ RBC PK activity.

TREATMENT

- Avoid oxidant stresses.
- Exchange transfusion (hyperbilirubinemia).
- Transfusion of packed RBCs if severe anemia or aplastic crisis.
- Splenectomy (after 5–6 years of age), if persistently severe anemia or frequent transfusion requirement, will ↑ reticulocyte count.
- Folate supplementation.

Hemolytic Membrane Defects

HEREDITARY SPHEROCYTOSIS

A 4-year-old boy has pallor and a family history of gallstone surgery. His Hgb is 8 g, retics 11, bili 2. *Think: Hereditary spherocytosis.*
Hereditary spherocytosis is a common inherited hemolytic anemia that is transmitted as an autosomal dominant. The characteristic feature is spherocytic red cells that are intrinsically defective. Hemolysis results in reticulocytosis and indirect hyperbilirubinemia. Splenomegaly and gallstones are common. Spherocytes are present in the peripheral blood smear. Splenectomy is helpful in reducing the rate of hemolysis.

DEFINITION

Red cell membrane defect → abnormally shaped erythrocytes and hemolysis.

ETIOLOGY

Genetic defect in erythrocyte membrane proteins, such as ankyrin.

PATHOPHYSIOLOGY

- Abnormal proteins cause destabilized RBC membrane—spherocytes.
- Abnormal RBCs become sequestered in the spleen and hemolyze.

EPIDEMIOLOGY

Autosomal dominant.

30% of cases are sporadic.

SIGNS AND SYMPTOMS

- Commonly asymptomatic.
- Neonatal jaundice.
- Evidence of hemolysis.
- Aplastic/hemolytic crisis.
- Splenomegaly.
- Gallstones.
- Leg ulcers.
- Chronic anemia.
- Positive family history.

DIAGNOSIS

- ↑ osmotic fragility.
- Spherocytes on peripheral film.
- Reticulocytosis.
- Hyperbilirubinemia.

TREATMENT

- Splenectomy (avoid or at least delay until >5 years old).
- Pneumococcal, meningococcal, and *Haemophilus influenzae* (Hib) vaccines before splenectomy.
- Treatment does not fix underlying RBC defect.

PAROXYSMAL NOCTURNAL HEMOGLOBINURIA

DEFINITION

- Complement-induced hemolytic anemia caused by acquired defect in RBC membrane.
- Red urine (intravascular hemolysis worse with relative hypoxia at night versus more concentrated urine at night).
- Thrombosis.

SIGNS AND SYMPTOMS

- Hemolysis worse during sleep → morning hemoglobinuria.
- Marrow failure.
- Intermittent or chronic hemolytic anemia.
- Leukopenia, thrombocytopenia.
- Complications can include thromboembolic phenomenon and acute myelogenous leukemia.

DIAGNOSIS

- ↑ LDG, ↓ haptoglobin, direct Coombs' is negative since hemolysis is not antibody directed.
- Sucrose lysis test, Ham's acid hemolysis test.
- Flow cytometry.

TREATMENT

- Prednisone.
- Bone marrow transplantation for severe disease.
- Splenectomy is not indicated.
- Eculizumab (humanized antibody which inhibits the activation of terminal complement components).
- Iron supplementation unless frequently transfused.
- Folic acid supplementation.

Aplastic Anemia

DEFINITION

- Rare group of closely related disorders → ↓ numbers of blood cells in each of the lines—RBCs, WBCs, and platelets (pancytopenia).
- Bone marrow is replaced with fat.

WARD TIP

Hereditary spherocytosis has the following characteristics: ↑ osmotic fragility, ↑ reticulocyte count, positive family history, and splenomegaly. Coombs' test is *not* positive.

WARD TIP

Splenectomy predisposes patients to overwhelming postsplenectomy infections (OPSIs) caused by encapsulated organisms:
- *Streptococcus pneumoniae*
- *Neisseria meningitidis*
- *Haemophilus influenzae*

WARD TIP

Onset of paroxysmal nocturnal hemoglobinuria is in late childhood.

ETIOLOGY

- Exact cause is unknown.
  - May be idiopathic.
  - Induced by drugs.
- Chemical exposure.
- Viral infection (hepatitis, EBV).
- Genetic causes (e.g., Fanconi anemia).

SIGNS AND SYMPTOMS

- Fatigue (fewer RBCs).
- Infections (fewer WBCs).
- Bleeding (fewer platelets).
- ↑ risk of leukemia.

DIAGNOSIS

- CBC—suspicious if at least two of the three cell lines are ↓.
- Bone marrow biopsy is definitive.
- Decreased reticulocyte count.

TREATMENT

- Platelet and RBC transfusions.
- Immunosuppressive drugs—antilymphocyte globulin (ALG), antithymocyte globulin (ATG), cyclosporine.
- Growth factors—erythropoietin (EPO), granulocyte colony-stimulating factor (G-CSF), granulocyte-macrophage colony-stimulating factor (GM-CSF).
- Stem cell transplantation is definitive cure but requires chemotherapy and/or radiation in preparation.

Thrombotic Thrombocytopenic Purpura (TTP)

DEFINITION

Hemolytic anemia that results from deposition of abnormal VWF multimers into microvasculature.

SIGNS AND SYMPTOMS

- Fever.
- Microangiopathic hemolytic anemia.
- Thrombocytopenia.
- Abnormal renal function.
- Neurologic signs.

DIAGNOSIS

- Normal prothrombin time (PT) and activated partial thromboplastin time (aPTT).
- Microangiopathic hemolytic anemia.
- Abnormal red cell morphology with schistocytes, spherocytes, helmet cells.
- ↑ reticulocyte count.
- Thrombocytopenia.

TREATMENT

- Plasmapheresis.
- Corticosteroids.
- Splenectomy.

Hemolytic-Uremic Syndrome (HUS)

👤 Ten days after an episode of viral diarrhea, a 2-year-old boy has pallor and icterus and petechiae of the skin and mucous membranes. His mother reports that he has not urinated for 24 hours. Characteristic lab findings include fragmented erythrocytes on smear, ↑ blood urea nitrogen (BUN), ↑ reticulocyte count, indirect hyperbilirubinemia, and normal platelet count. *Think: HUS.*

HUS is a common cause of renal failure in children. Triad: microangiopathic hemolytic anemia, thrombocytopenia, and uremia. Onset is usually preceded by gastroenteritis. It may be epidemic during summer months. Platelet count is usually low, but may be normal early in the course of illness.

ETIOLOGY

Acute gastroenteritis caused by *Escherichia coli* O157:H7 (produces a shiga-like toxin).

SIGNS AND SYMPTOMS

- Hemolytic anemia.
- Thrombocytopenia.
- Acute renal failure (ARF).

DIAGNOSIS

- History of bloody diarrhea.
- Abnormal red cell morphology.
- Thrombocytopenia with normal megakaryocytes in marrow.
- Urine—protein, RBCs, and casts.

TREATMENT

- Fluid management.
- Dialysis.
- Plasmapheresis (for neurologic complications).
- Antibiotics not indicated.

IMMUNE THROMBOCYTOPENIC PURPURA (ITP)

👤 A 4-year-old previously healthy girl with purple skin lesions had a visit to the ED with an upper respiratory infection (URI) a month ago. CBC is normal except for low platelets. *Think: ITP.*

Typical presentation: Sudden onset of generalized petechiae and purpura in a previously healthy child. Often, there is a history of a viral infection weeks before the onset. Physical examination is usually normal except petechiae and purpura. Complete remission occurs in most children.

DEFINITION

- Acquired hemorrhagic disorder that results from excessive destruction of platelets—typically benign.
- Acute (remission within 6 months).
- Chronic (>6 months).
- Also called autoimmune thrombocytopenic purpura.

EXAM TIP

ITP is the most common thrombocytopenia of childhood.

ETIOLOGY

- Unknown.
- Associated with antecedent viral illnesses in 50–65% of cases.

PATHOPHYSIOLOGY

- Immune mechanism—autoantibodies.
- Sensitization.
- Antibody binds to the platelet membrane and results in splenic destruction of antibody-coated platelets.

SIGNS AND SYMPTOMS

- Abrupt onset of petechial, purpura, and epistaxis.
- Usually 1–4 weeks after a viral infection.
- <1% of patients with acute ITP will have intracranial bleed.

DIAGNOSIS

- Diagnosis of exclusion.
- WBC and Hgb levels normal.
- Normal peripheral smear except thrombocytopenia.
- Bone marrow (not always indicated).
- Normal erythrocytic and granulocytic series.
- Normal or ↑ megakaryocytes.

TREATMENT

- Treatment based on severity of bleeding.
- Admit if platelet count is <20.
- >80% recover within several months without treatment.
- Intravenous immune globulin (IVIG) or anti-Rho antibodies.
- Intravenous methylprednisolone.
- Splenectomy if:
  - Older children (>4 years).
  - Severe ITP.
  - Chronic ITP (>1 year).
- Platelet transfusion generally not helpful.

Disseminated Intravascular Coagulation (DIC)

DEFINITION

↑ fibrinogenesis and fibrinolysis.

ETIOLOGY

- Sepsis.
- Incompatible transfusion.
- Rickettsial infection.
- Snake bite.
- Acute promyelocytic leukemia.

PATHOPHYSIOLOGY

- Hypoxia.
- Acidosis.
- Tissue necrosis.
- Shock.
- Endothelial damage.

Signs and Symptoms

- Bleeding.
- Petechiae and ecchymoses.
- Hemolysis.

Diagnosis

- ↑ PT and aPTT.
- ↓ fibrinogen and platelets.
- ↑ fibrin degradation products and D-dimer.

Treatment

- Treat underlying cause.
- Replacement therapy:
  - Platelets (thrombocytopenia).
  - Cryoprecipitate (hypofibrinogenemia).
  - Fresh frozen plasma (FFP) (replacement of coagulation factors).
- Heparin prevents consumption of coagulation factors.

Coagulation Disorders

- Bleeding due to platelet problems usually occurs immediately and is mucocutaneous.
- Bleeding due to factor deficiencies is often "deeper" bleeding (intra-articular, intramuscular).
- See Table 15-5.

VON WILLEBRAND DISEASE

A child presents with epistaxis, prolonged bleeding time, and a normal platelet count. *Think: von Willebrand disease.*

von Willebrand disease is the most common inherited bleeding disorder. A family history of an established bleeding disorder should be sought. Typical presentation: Mucocutaneous bleeding (excessive bruising, epistaxis, and menorrhagia). The evaluation involves qualitative and quantitative measurements of von Willebrand factor (vWF).

Definition

Most common hereditary bleeding disorder, seen in up to 1% of population, resulting from deficiency of vWF (qualitative or quantitative).

Etiology

- Autosomal dominant—chromosome 12.
- Deficiency of factor VIII-R.
- Males = Females.

Pathophysiology

Defective platelet function due to ↓ in level or function of von Willebrand cofactor.

Signs and Symptoms

- Easy bruising.
- Heavy or prolonged menstruation.

TABLE 15-5. Coagulation Tests

TEST	PURPOSE	
PT (INR)	Extrinsic system	Elevated in DIC, warfarin use, liver failure, myelofibrosis, vitamin K deficiency, fat malabsorption, circulating anticoagulants, factor deficiencies
aPTT	Intrinsic	Elevated in factor deficiencies, circulating anticoagulants, heparin use, higher doses of warfarin
Bleeding time	Surgical	Related to platelet count
		If lengthened and platelet count is normal, consider qualitative platelet defect
Platelet count	Related to bleeding time	$<100,000/mm^3$—mild prolongation of bleeding time
		<50,000—easy bruising
		<20,000—↑ incidence of spontaneous bleeding
Platelet aggregation	Qualitative	May be abnormal even with normal platelet count—qualitative platelet disorders (Glanzmann's thrombasthenia), von Willebrand factor deficiency
Fibrin degradation products	Fibrin activation	Elevated in DIC, trauma, inflammatory disease
D-dimer	Intravascular fibrinolysis	Present in most individuals, especially with cancer, trauma
		Sensitive for active clotting, but not specific
Assays for specific factors	Quantitative	Hemophilia A (VIII), hemophilia B (IX), von Willebrand factor deficiency (VIII, vWF)

aPTT, activated partial thromboplastin time; DIC, disseminated intravascular coagulation; INR, International Normalized Ratio; PT, prothrombin time.

WARD TIP

Avoid aspirin and nonsteroidal anti-inflammatory drug (NSAID) use in patients with von Willebrand disease.

WARD TIP

Patient should have therapeutic trial of DDAVP to measure response before use.

EXAM TIP

Side effects of DDAVP: Tachyphylaxis and hyponatremia.

- Frequent or prolonged epistaxis.
- Prolonged bleeding after injury, surgery (circumcision), or invasive dental procedures.

DIAGNOSIS

- Obtain family or personal history of bleeding episodes.
- aPTT normal or prolonged.
- Prolonged bleeding time.
- Normal PT.
- Abnormal factor VIII clotting activity.
- Quantitative assay for vWF antigen.
- Reduced ristocetin cofactor activity.
- Abnormal platelet aggregation tests.
- Normal platelet count.

TREATMENT

- Usually no therapy necessary.
- Avoid unnecessary trauma.
- Desmopressin (DDAVP), factor VIII for surgery if needed.
- Cryoprecipitate recommended only in life-threatening emergencies due to the risk of human immunodeficiency virus (HIV) and hepatitis infection.
- Recombinant vWF before major surgery or bleeding.

FACTOR VIII REPLACEMENT

Bleeding Time	Desired Level (%) VIII
Hematoma	20–40%
Dental extraction	50%
Head injury	100%
Major surgery	100%

HEMOPHILIA

DEFINITION

- Inherited coagulation defects.
- Hemophilia A: Factor VIII deficiency.
- Hemophilia B: Factor IX deficiency.
- Hemophilia A is more common than hemophilia B.
- Hemophilia A is more likely to be severe.

PATHOPHYSIOLOGY

Slowed rate of clot formation.

SIGNS AND SYMPTOMS

- Easy bruising.
- Intramuscular hematomas.
- Hemarthroses (hemorrhage into a joint -ankles, then knees and elbows) → joint destruction if untreated.
- Spontaneous hemorrhaging if levels <5%. Severe disease more likely to have spontaneous bleeding.

DIAGNOSIS

- Family history.
- aPTT 2–3 times upper limit of normal.
- Normal PT.
- Normal platelet.
- Specific factor assays.

TREATMENT

- Early diagnosis.
- Prevent trauma.
- Prompt management of bleeding.
- Recombinant factors (prophylactic versus on-demand).
- Cryoprecipitate.
- Beware of transfusion complications, including disease transmission.
- Avoid certain medications (anticoagulants, aspirin, NSAIDs).

Hypercoagulable States

DEFINITION

Predisposition to thrombosis.

PATHOPHYSIOLOGY

Primary (inherited) or secondary (acquired) disturbances in the three areas of Virchow's triad:
- Endothelial damage (e.g., inflammation, trauma, burns, infection, surgery, central lines, artificial heart valves).

EXAM TIP

Hemophilia A and hemophilia B are X-linked recessive diseases that present in male children of carrier females.

WARD TIP

Patients with hemophilia may lose large amounts of blood into an iliopsoas hematoma.

WARD TIP

Severe hemophilia <1% of factor activity.

EXAM TIP

Only 30% of male infants with hemophilia bleed at circumcision.

EXAM TIP

aPTT corrects in mixing studies.

WARD TIP

- 1 unit of VIII/kg—↑ 2%
- 1 unit of IX/kg—↑ 1%

- Change in blood flow (e.g., immobilization, local pressure, congestive heart failure [CHF], hypovolemia, hyperviscosity, pregnancy).
- Hypercoagulability (e.g., factor release secondary to surgery, trauma, malignancy); antiphospholipid antibodies, lupus, oral contraceptive use; genetic predispositions such as deficiencies of protein S, protein C, antithrombin III, or factor V Leiden; nephrotic syndrome, polycythemia vera, sickle cell anemia, homocystinemia, fibrinogenemia.

SIGNS AND SYMPTOMS

- Deep vein thrombosis (DVT).
- Pulmonary embolism (PE).
- Myocardial infarction (MI).
- Stroke.
- Recurrent pregnancy loss.

DIAGNOSIS

- Family history.
- Patient history of recurrent, early, unusual, or idiopathic thromboses.
- Appropriate screening.
- Risk factor assessment.

TREATMENT

- Reduce risk factors—mobilize patients, encourage to quit smoking and alcohol, hydrate.
- Aspirin, heparin, warfarin, etc., as appropriate.

Malaria

👤 An 8-year-old American-born boy of Somali parents presents with fever for 1 week after returning from his vacation. On examination he has splenomegaly. *Think: Malaria.* Malaria should be considered in any child who presents with fever and has traveled or resided in a malaria-endemic area. It is characterized by fever, chills, sweats, fatigue, anemia, and splenomegaly. The diagnosis is established by identification of organisms on peripheral smear.

DEFINITION

Blood-borne parasite infection.

ETIOLOGY

- Transmitted by female *Anopheles* mosquito.
- Four species of *Plasmodium:*
  - *P. falciparum.*
  - *P. malariae.*
  - *P. ovale.*
  - *P. vivax.*

EPIDEMIOLOGY

Most frequent cause of hemolysis worldwide.

SIGNS AND SYMPTOMS

- Fever.
- Chills.

- Jaundice.
- Splenomegaly.
- Sweats.

DIAGNOSIS

- Traditional method: Identification of organisms on thick and thin periph-eral blood smears obtained when patient is acutely febrile.
- Newer methods include polymerase chain reaction (PCR) and immunoassays.

TREATMENT

- See CDC Web site for specific guidelines—usually dependent on resis-tance in geographic location.
- Chloroquine is used for *P. ovale, P. vivax, P. malariae,* and chloroquine-sensitive *P. falciparum.*
- Significant areas of chloroquine-resistant *P. falciparum* exist. In these places, mefloquine or atovaquone-proguanil should be used.

Transfusion Reactions

EPIDEMIOLOGY

- Approximately 4% of transfusions are associated with some form of adverse reaction.
- Most are febrile nonhemolytic or urticarial.
- See Table 15-6.

INDICATIONS FOR TRANSFUSION OF BLOOD PRODUCTS

- Packed RBCs: Hgb <8 or 8–10 if symptomatic.
- Platelets: <10,000/μL; 10,000–50,000 if bleeding; <75,000 in preparation for surgery.
- FFP: Treatment of bleeding from vitamin K deficiency, ↑ International Normalized Ratio (INR), liver disease, or during plasma exchange for TTP.
- Cryoprecipitate: Hypofibrinogenemia, hemophilia A, vWF deficiency, fac-tor XIII deficiency.

COMPLICATIONS

- Hemolytic, febrile, and allergic reactions.
- Transfusion-related acute lung injury (TRALI).
- Disease transmission (e.g., HIV, hepatitis B virus [HBV], hepatitis C virus [HCV], human T-lymphotropic virus [HTLV], cytomegalovirus [CMV], parvovirus).
- Iron overload, electrolyte disturbances.
- Fluid overload, hypothermia.

> **WARD TIP**
>
> Children rarely have febrile reactions to initial transfusion unless they are immunoglobulin A (IgA) deficient.

> **WARD TIP**
>
> Life-threatening transfusion reactions are nearly always due to clerical errors (wrong ABO blood type).

Methemoglobinemia

ETIOLOGY

- Congenital.
  - Deficiency of cytochrome b5 reductase.
  - Hgb M disease—inability to convert methemoglobin back to hemoglobin.

T A B L E 1 5 - 6 . Transfusion Reactions

Type	Etiology	Signs and Symptoms	Treatment	Prevention
Acute hemolytic (1 in 15,000–36,000) (fatal 1 in 630,000)	RBC incompatibility	Fever, chills, nausea	Stop transfusion	Pretransfusion testing
	Damaged RBCs	Chest/arm/back pain	Manage blood pressure and renal perfusion	Accurate labeling, unit inspection
	Hypotonic solution	Hemoglobinuria, oliguria Shock, hypotension DIC Dyspnea	Control DIC	Proper patient identification
Delayed hemolytic	Antibodies to minor blood group antigens during prior transfusion (Kidd, Duffy, Rh, Kell)	3–10 days post-transfusion	Usually self-limited	Chronically transfused patients should received leukocyte reduced products
		Falling hematocrit, fever, hyperbilirubinemia/uria	Supportive	
Allergic (1 in 30–100)	Antibodies to plasma proteins	Hives, itching, local erythema	Antihistamines	Pretransfusion antihistamines Washed cellular blood products
Anaphylactic (1 in 18,000–170,000)	Antibodies to IgA	Cough, respiratory distress, bronchospasm Nausea, vomiting, abdominal cramps, diarrhea Shock, vascular instability, loss of consciousness	Stop transfusion Epinephrine Supportive care	IgA-deficient plasma products Washed cellular blood products
Febrile nonhemolytic (1 in 50–100)	Antibodies to granulocytes	Fever, chills	Stop transfusion	Pretransfusion antipyretics
		Dyspnea, anxiety	Demerol	
	Cytokines in plasma		Antipyretics	Leukocyte-reduced blood products
Transfusion-related acute lung injury (TRALI) (1 in 5000–10,000)	Antigranulocyte antibodies in donor product	Bilateral pulmonary edema Cyanosis, hypoxemia Respiratory distress, cough Hypotension, normal central venous pressure ARDS-like picture Fever, chills	Supportive	Do not use plasma products from implicated donor

T A B L E 1 5 - 6 . **Transfusion Reactions (*continued*)**

TYPE	ETIOLOGY	SIGNS AND SYMPTOMS	TREATMENT	PREVENTION
Circulation overload	Hypervolemia	Dyspnea, cyanosis, hypoxemia	Diuretics	Pretransfusion diuretics
	Rapid infusion		Oxygen	Slow infusion
	CHF	Tachycardia, hypertension	Phlebotomy	Limit volume
		Pulmonary edema, cough		

ARDS, adult respiratory distress syndrome; CHF, congestive heart failure; DIC, disseminated intravascular coagulation; IgA, immunoglobulin A; RBC, red blood cell.

- Acquired—↑ production of methemoglobin:
  - Typically results from ingestion of specific drugs or agents that cause an increase in production of methemoglobin (nitrites [contaminated water], xylocaine/benzocaine [teething gel], sulfonamides, benzene, aniline dyes, potassium chlorate).

PATHOPHYSIOLOGY

- Altered state of hemoglobin (ferrous irons of heme (Fe^{++}) are oxidized to ferric (Fe^{+++})).
- Methemoglobin iron is in ferric form ($<2\%$) and is unable to transport oxygen.

SIGNS AND SYMPTOMS

Depends on the concentration:
- 10–30%: Cyanosis.
- 30–50%: Dyspnea, tachycardia, dizziness.
- 50–70%: Lethargy, stupor.
- >70%: Death.

DIAGNOSIS

Methemoglobin level—co-oximetry studies.

TREATMENT

- Concentration dependent.
- <30%: Treatment not needed.
- 30–70%: IV methylene blue.
- Hyperbaric O_2.
- Oral ascorbic acid (200–500 mg).

> **WARD TIP**
>
> Suspect methemoglobinemia if:
> - Oxygen-unresponsive cyanosis
> - Chocolate brown blood

Porphyria

DEFINITION AND ETIOLOGY

Porphyria refers to a group of disorders (inherited and acquired) characterized by an inherited deficiency of the heme biosynthetic pathway.

SIGNS AND SYMPTOMS

- Acute (hepatic) porphyria: Abdominal pain, vomiting, neuropathy, mental disturbances, seizures, autonomic nervous system dysfunction, cardiac arrythmias, tachycardia; ↑ risk of hepatocellular carcinoma over lifetime.
- Cutaneous (erythropoietic) porphyria: Edema, blister formation, ↑ hair growth, photosensitivity, red urine.
- Precipitated by drugs, infection.

DIAGNOSIS

- Spectroscopy: Blood, urine, stool.
- Hyponatremia/syndrome of inappropriate antidiuretic hormone secretion (SIADH).
- Renal insufficiency.
- Serum/urine porphyrin levels.
- Measurement of porphyrin precursors ALA and PBG.

TREATMENT

- For acute attacks: Analgesia, hydration, maintain electrolytes, IV hematin especially if low serum sodium or status epilepticus, high-carbohydrate diet, glucose 10% infusion.
- Long-term management:
  - Avoid alcohol and all drugs that can precipitate an attack.
  - Sunscreen.

Disorders of White Blood Cells

NEUTROPENIA

DEFINITION

Absolute neutrophil count (ANC) <1500/mm^3:
- Mild: 1000–1500.
- Moderate: 500–1000.
- Severe: <500.

ETIOLOGY

- Congenital.
- Kostmann syndrome.
- Schwachman syndrome.
- Fanconi syndrome.
- Acquired.
- Infection.
- Immune.
- Hypersplenism.
- Drugs.
- Aplastic anemia.
- Vitamin B$_{12}$, folate, or copper deficiency.

SIGNS AND SYMPTOMS

- ↑ susceptibility to bacterial infection.
- Stomatitis, gingivitis, recurrent otitis media, cellulitis, pneumonia, and septicemia.

Leukemia

A 3-year-old girl has had fever, anorexia, and fatigue for the past month. She has lost 5 kg. She has pallor, cervical adenopathy, splenomegaly, skin ecchymoses, and petechiae. *Think: Acute leukemia.*

Typical presentation: Pancytopenia—anemia (pallor and fatigue), thrombocytopenia (epistaxis, ecchymoses, and petechiae), and white cell may be low (sepsis) or high. Initial presentation may be nonspecific and subtle and develop over weeks to months. Final diagnosis depends on the results of bone marrow aspirate and biopsy.

EPIDEMIOLOGY

- Leukemia is the most common malignancy in children, followed by brain tumors.
- 30% of all childhood malignancies.
- ALL is five times more common than AML.

RISK FACTORS

- Trisomy 21.
- Fanconi anemia.
- Bloom syndrome.
- Immune deficiency.
- Wiskott-Aldrich syndrome.
- Agammaglobulinemia.
- Ataxia–telangiectasia.

SIGNS AND SYMPTOMS

- Fever.
- Pallor.
- Bleeding.
- Bone pain.
- Abdominal pain.
- Lymphadenopathy.
- Hepatosplenomegaly.

ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)

DEFINITION

Malignant disorder of lymphoblasts.

EPIDEMIOLOGY

- Most common malignancy in children.
- Eighty percent of leukemia in children.

SIGNS AND SYMPTOMS

- Fatigue, anorexia, lethargy, pallor.
- Bone pain.
- Fever.
- Bleeding, bruising, petechiae.
- Lymphadenopathy.
- Hepatosplenomegaly.
- Bone tenderness.

WARD TIP

70–80% of childhood ALL are of the precursor B cell lineage.

- Testicular swelling.
- Septicemia.

DIAGNOSIS

- CBC: Anemia, abnormal white count, low platelet count.
- Electrolytes, calcium, phosphorus, uric acid, lactic dehydrogenase (LDH).
- Chest x-ray (mediastinal mass).
- Bone marrow—hypercellular, ↑ lymphoblasts.
- Cerebrospinal fluid (CSF)—blasts.
- Cytogenetics for risk stratification.

TREATMENT

- Four phases:
    - Remission induction: Cytoxan, vincristine, prednisone, L-asparaginase, and/or doxorubicin.
    - Consolidation: May add 6MP, 6TG, or cytosine arabinoside.
    - Maintenance therapy: 2 years—methotrexate and 6MP, may add vincristine and prednisone.
    - CNS prophylaxis: Methotrexate to CSF, may have radiation to the head.
- Infection prevention—antibiotics, isolation if necessary.
- `Watch for tumor lysis syndrome.

ACUTE MYELOGENOUS LEUKEMIA (AML)

DEFINITION

Malignant proliferation of immature granular leukocytes.

EPIDEMIOLOGY

- Fifteen to twenty percent of leukemia cases.
- Occurs primarily in children <1-year-old.
- One in 10,000 people.

ETIOLOGY

Predisposing factors:
- Trisomy 21.
- Diamond-Blackfan syndrome.
- Fanconi anemia.
- Bloom syndrome.
- Kostmann syndrome.
- Toxins such as benzene.
- Immunosuppression.
- Polycythemia vera.

SIGNS AND SYMPTOMS

- Manifestations of anemia, thrombocytopenia, or neutropenia, including fatigue, bleeding, and infection.
- Chloroma—localized mass of leukemic cells.
- Bone/joint pain.
- Hepatosplenomegaly.
- Lymphadenopathy.

DIAGNOSIS

- >25% myeloblasts in the bone marrow, hypercellular.
- Abnormal white count, platelet count, and anemia.
- Bone destruction and periosteal elevation on x-ray.

TREATMENT

- Two phases:
    - Remission induction: 1 week—anthracycline (daunorubicin) and cytosine arabinoside (cytarabine).
    - Postremission therapy: Several more courses of high-dose cytarabine chemotherapy, allogenic stem cell transplant, or autologous stem cell transplant.
- Infection prevention—isolation, antibiotics.
- RBC transfusions for anemia.
- Platelet transfusions for bleeding.
- Complete remission in 70–80%.

CHRONIC MYELOGENOUS LEUKEMIA (CML)

DEFINITION

- Clonal disorder of the hematopoietic stem cell with Philadelphia chromosome translocation—t(9;22)(q34;q11).
- Uncontrolled production of mature and maturing granulocytes, predominantly neutrophils.

EPIDEMIOLOGY

Tends to occur in middle-aged people.

SIGNS AND SYMPTOMS

- Insidious onset.
- Splenomegaly (massive).
- Fever, bone pain, sweating.

TREATMENT

- Hydroxyurea.
- α-Interferon.
- Bone marrow transplant.
- Radiation.

JUVENILE CHRONIC MYELOGENOUS LEUKEMIA (JCML)

DEFINITION

- Clonal condition involving pluripotent stem cell.
- <2 years.

EPIDEMIOLOGY

Ninety-five percent diagnosed before age 4.

SIGNS AND SYMPTOMS

- Skin lesions (eczema, xanthoma, café au lait spots).
- Lymphadenopathy.
- Hepatosplenomegaly.

DIAGNOSIS

- Monocytosis.
- ↑ marrow monocyte precursors.
- Philadelphia chromosome absent.
- Blast count.

WARD TIP

CML often gets diagnosed when CBC shows elevated WBCs.

EXAM TIP

Neurofibromatosis is associated with an ↑ incidence of JCML and leukemia.

- <5% (peripheral blood).
- <30% (marrow).

TREATMENT

- Complete remissions have occurred with stem cell transplant.
- Majority relapse, with overall survival of 25%.

LYMPHOMA

Most common childhood cancer in 15- to 19-year-old age group.

DEFINITION

- Lymphoid malignancy arising in a single lymph node or lymphoid region (liver, spleen, bone marrow).
- Hodgkin.
- Nodular sclerosing (46%—most common).
- Mixed cellularity (31%).
- Lymphocyte predominance (16%).
- Lymphocyte depletion (7%).
- Non-Hodgkin (10% of all pediatric tumors).
- Lymphoblastic.
- Burkitt's (39%).
- Large cell or histiocytic.

SIGNS AND SYMPTOMS

- Fever, night sweats.
- Weight loss, loss of appetite.
- Cough, dysphagia, dyspnea.
- Lymphadenopathy—lower cervical, supraclavicular.
- Hepatosplenomegaly.
- Mediastinal mass.

DIAGNOSIS

- CBC, erythrocyte sedimentation rate (ESR).
- Serum electrolytes, uric acid, LDH.
- Chest x-ray.
- Computed tomography (CT) of chest, abdomen, and pelvis.
- Lymph node or bone marrow biopsy.

STAGING

- Stage I: One lymph node involved.
- Stage II: Two lymph nodes on same side of diaphragm.
- Stage III: Lymph node involvement on both sides of diaphragm.
- Stage IV: Bone marrow or liver involvement.

TREATMENT

- Radiation for stage I or II disease.
- Chemotherapy for stage III or IV.

WARD TIP

Reed-Sternberg cells are characteristic of Hodgkin lymphoma.

WARD TIP

Four histological classifications:
- Nodular sclerosis
- Mixed cellularity
- Lymphocyte depleted
- Lymphocyte rich

WARD TIP

Suspicious lymph nodes are:
- Painless, firm, and rubbery
- In the posterior triangle

Endocrine Disease

DISORDERS OF GLUCOSE HOMEOSTASIS

Diabetes Mellitus

> 👤 A 10-year-old girl has blood glucose of 300 mg/dL and a large amount of glucose and trace ketones in her urine. She has lost 1 kg of weight with polyuria and polydispsia for the past few weeks. *Think: Type 1 diabetes.*
> A 16-year old obese male with blood sugar of 300mg/dL with a thickened rash noted on the back of his neck. *Think: Type 2 diabetes.*
> Typical history: Polyuria, polydipsia, polyphagia, and weight loss over a period of time. The initial symptoms due to hyperglycemia may be nonspecific. Exogenous insulin is required to correct the metabolic derangement due to insulin deficiency. Children with type 2 diabetes mellitus are usually overweight and may show signs of insulin resistance such as acanthosis nigricans. Family history of type 2 diabetes in first- and second-degree relative may also be present.

See Table 16-1.

DEFINITION

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels.

> ✋ **WARD TIP**
>
> Think of testing urine glucose with the onset of enuresis in a previously toilet-trained child.

TABLE 16-1. Diabetes

TYPE I (INSULIN DEPENDENT)	TYPE II (NON-INSULIN DEPENDENT)
Absolute insulin deficiency (require insulin for survival)	Insulin is ↑, normal, or ↓ (insulin is not required for survival)
Immune mediated	Insulin resistance
Juvenile onset	Usually adult onset but incidence is rising in children
Shorter duration of symptoms with history of weight loss at diagnosis	Mild symptoms, 85% overweight at diagnosis
Ketosis common	Ketosis infrequent but occurs under stressful conditions
DKA is a complication of uncontrolled diabetes	Hyperglycemic hyperosmolar state is a rare complication
HLA-DR3 and HLA-DR4 (chromosome 6)	Not HLA associated
5% have diabetic relative	74–100% have a diabetic relative

DKA, diabetic ketoacidosis; HLA, human leukocyte antigen.

EPIDEMIOLOGY

- Diabetes is one of the most common endocrine disorders of the pediatric age group.
- Classification:
    - **Type 1 diabetes:** Caused by ABSOLUTE insulin deficiency. It usually presents with classic symptoms of polyuria, polydipsia, polyphagia, and weight loss. Most children have positive urine ketones at onset. It may also present as diabetic ketoacidosis or may be an incidental discovery. Incidence is roughly 1 in 400 children. It is prevalent in Caucasians of northern European descent and caused by autoimmune destruction of pancreatic islet cells. Over 80% of children are positive for immune markers of beta cell destruction (examples: islet cell antibodies, antiglutamic acid decarboxylase antibodies, and insulin autoantibody).
    - **Type 2 diabetes:** A heterogeneous disorder characterized by insulin resistance and hyperglycemia as well as RELATIVE insulin deficiency (impaired secretion). It is insidious in onset and diagnosis is usually delayed because of lack of symptoms early in the course of disease. It is prevalent in certain minorities such as Hispanic-American, Native American, African-American, Asian-American, and Pacific Islanders. Its incidence is increasing in children due to the rise in childhood obesity. Most of them have acanthosis nigricans (velvety hyperpigmented thickening of skin in intertriginous sites such as neck and axillae), which is a cutaneous manifestation of insulin resistance.

> **EXAM TIP**
>
> The prevalence of type 1 diabetes is rising particularly in those under the age of 5 years for unclear reasons. The prevalence of type 2 diabetes is increasing in children secondary to increasing prevalence of childhood obesity.

PATHOPHYSIOLOGY

Revolves around relative insulin deficiency or insulin resistance leading to:
- ↓ glucose utilization.
- ↑ hepatic glucose production → hyperglycemia.

SIGNS AND SYMPTOMS

- Triad of polyuria, polydipsia, and polyphagia (more abrupt in type 1 diabetes).
- Weight loss and enuresis are common symptoms in type 1 diabetes.
- Vomiting, dehydration, and abdominal pain are hallmark of acute complication → diabetic ketoacidosis.

DIAGNOSIS

- Fasting blood glucose ≥126 mg/dL (7 mmol/L).
- Random blood glucose ≥200 mg/dL along with symptoms of diabetes.
- Two-hour plasma glucose >200 mg/dL during a 75-g oral glucose tolerance test.
- Hemoglobin A1C ≥6.5 percent on two occasions.
- To diagnose type 2 diabetes early in children, the American Diabetes Association recommends screening children beginning 10 years of age or puberty (whichever comes first) and repeating every 3 years. Testing should be done sooner if they are overweight (BMI > 85th percentile but < 95th percentile) or obese (BMI > 95th percentile) and have two or more risk factors such as:
    - Family history of type 2 diabetes (first- and second-degree relatives).
    - Race (Native American, African-American, Hispanic, and Asian-American or Pacific Islander).
    - Signs and symptoms associated with insulin resistance (acanthosis nigricans, dyslipidemia, hypertension [HTN], polycystic ovarian syndrome, or small-for–gestational-age birth weight).
    - Maternal history of diabetes or gestational diabetes.

TREATMENT

- Patient education and counseling.
- Insulin is the mainstay of treatment in type 1 diabetes, without which the disease is rapidly fatal. In addition, diabetic and nutrition counseling is required to promote adherence to treatment plans and to ensure normal quality of life with minimal complications.
- Oral hypoglycemics in type 2 diabetes (such as metformin, sulfonylureas, thiazolidinediones) along with diet and exercise are important in the management of type 2 diabetes.

Diabetic Ketoacidosis (DKA)

A 3½-year-old boy is found unconscious. He has a flushed face, pulse of 160/min, respiratory rate of 30/min with shallow breaths, blood pressure 40/20 mm Hg, and an unusual odor on his breath. He is difficult to arouse. His mucous membranes are dry. His parents report a weight loss of 5 lb in the past month and noted that he was drinking a lot more than usual. *Think: DKA,* and check serum glucose.

Diabetic ketoacidosis (DKA) is an acute, major life-threatening complication of diabetes and mainly occurs in type 1 diabetes in which a complex disordered metabolic state of hyperglycemia, ketoacidosis, and ketonuria occurs. Weight loss is due to hyperglycemia and glucosuria → lipolysis. Ketosis also leads to anorexia and nausea contributing to weight loss. Shallow breathing is a respiratory compensation for metabolic acidosis secondary to ketoacid accumulation. Severe dehydration is due to glucosuria → osmotic diuresis and volume depletion.

DEFINITION

- Hyperglycemia >200 mg/dL.
- Acidosis pH < 7.30.
- Bicarbonate <15 mmol/L.
- Beta hydroxybutyrate >3 mmol/L.

ETIOLOGY/PATHOPHYSIOLOGY

- ABSOLUTE insulin deficiency → accelerated hepatic and renal glucose production and impaired glucose utilization, release of free fatty acids into circulation (from lipolysis) and ↑ fatty acid oxidation to ketone bodies → ketosis and hyperglycemia.
- Precipitating factors—stress, infection, trauma.

SIGNS AND SYMPTOMS

Polyuria, polydipsia, dehydration, weight loss, fatigue, headache, nausea, vomiting, abdominal pain, tachycardia, tachypnea (Kussmaul breathing).

OTHER LABORATORY FINDINGS

- ↑ anion gap (>12–16 mEq).
- ↑ hemoglobin (Hgb) and hematocrit (Hct) (hemoconcentration).
- ↑ white blood cell (WBC) count.
- ↓ serum sodium (Na) (pseudohyponatremia from hyperglycemia and/or hypertriglyceridemia).
- Normal or ↑ potassium (K) (from shift of K from intracellular to extracellular compartment due to acidosis).

> **EXAM TIP**
>
> Insulin-dependent diabetes mellitus in children is associated with islet cell antibodies and ↑ prevalence of human leukocyte antigen (HLA)-DR3 and HLA-DR4 or both.

> **WARD TIP**
>
> Dehydration in DKA is primarily intracellular and is often underestimated.

- Normal or ↑ phosphate (from shift of K from intracellular to extracellular compartment due to acidosis).
- Urinalysis reveals glucose and ketones.

TREATMENT

- Careful fluid and electrolyte replacement to avoid cerebral edema. Rehydration fluid should not exceed 3000 mL/m^2/day.
- Initial bolus should be 10 mL/kg normal saline. Repeat bolus if needed. Subsequent replacement fluid can be 0.45% or 0.9% saline with potassium.
- Potassium should be given as potassium chloride AND potassium phosphate.
- Insulin regular (0.1 U/kg/hr).
- Glucose (add glucose to IV fluids when blood glucose is <250–300 mg/dL).

COMPLICATIONS

- Hypoglycemia.
- Hypokalemia.
- Cerebral edema: Cause of death in patients with DKA (symptoms such as headache/mental status changes may be indicative of acute intracranial pressure elevation). Treatment includes 3% saline (hypertonic saline) administration, and/or mannitol 0.5–2 g/kg every 4–6 hours as needed.

Hypoglycemia

A 14-year-old boy with an 8-year history of diabetes mellitus has had frequent admissions for DKA in the past 18 months. His school performance has been deteriorating. Recently, he has had frequent episodes of hypoglycemia. He is Tanner stage 2 in pubertal development, and has mild hepatomegaly. *Think: Poorly controlled diabetes mellitus due to noncompliance.*

Adolescence is a difficult age for management of any chronic disease such as diabetes. Not adhering to the treatment regimen is common in teenagers. Often, blood sugar levels are high because of missing the dose of insulin. However, inappropriate administration of insulin doses may result in secondary hypoglycemia. Recurrent hospitalization is the hallmark of noncompliance. Hepatomegaly is most likely due to poorly controlled diabetes mellitus

ETIOLOGY

- Hyperinsulinism.
- Hormone deficiencies (glucocorticoid, growth hormone).
- Glycogen storage disease.
- Defect in gluconeogenesis.
- Fatty acid oxidation defects.
- Organic acidemias.
- Ketotic hypoglycemia.
- Malnutrition, prematurity, SGA.
- Liver failure.
- Congenital heart diseases.
- Tumors.
- Poisons/drugs (salicylates, alcohol).
- Systemic disease—sepsis, burns, cardiogenic shock.

TREATMENT

- Acute symptomatic hypoglycemia: If patient is conscious and able to drink, rapidly absorbed carbohydrates should be given by mouth, e.g., fruit juice at a dose of 0.3 g/kg glucose. In children with altered level of consciousness, IV dextrose should be administered (2.5 mL/kg $D_{10}W$) over 10 minutes to restore plasma glucose concentration to normal, followed by 10% dextrose at 6–8 mg/kg/min.
- In patients with hyperinsulinemia, subcutaneous glucagon (0.03 mg/kg) can reverse the hypoglycemia.

Hyperinsulinism

A 2-hour-old newborn has plasma glucose of 20 mg/dL. Physical examination shows a large plethoric newborn. Birth weight is >90th percentile. *Think: Hyperinsulinism.*

Hyperinsulinism is a common cause of hypoglycemia in early infancy. These infants may have macrosomia. Hypoglycemia may develop on the first day of life, and there may be rapid development after a few hours of feeding. The diagnostic criterion is the presence of signs and symptoms of hypoglycemia with low plasma glucose level and an inappropriately elevated insulin level. Macrosomia is due to hyperinsulinemia, as insulin is an important growth factor in intrauterine life. Transient hyperinsulinism may occur due to maternal diabetes. Persistent hyperinsulinism is an autosomal recessive genetic disorder.

EPIDEMIOLOGY

Hyperinsulinemia is the most common cause of severe hypoglycemia in early infancy. Sixty percent develop hypoglycemia during the first month of life, 30% in the first year. Clinical manifestations of hypoglycemia may include jitteriness/tremors, sweating, irritability, pallor, tachypnea, poor suck or feeding. In severe hypoglycemia changes in level of consciousness and seizures may be seen.

TRANSIENT HYPERINSULINEMIA

- Excessive insulin secretion in infants from transient dysfunction in islet cell function.
- Inadequate glucose supply (inadequate glycogen stores, impaired glucose production).
- Risk factors include:
  - Small for gestational age (SGA), large for gestational age (LGA), or premature infants.
  - Perinatal hypoxia/asphyxia.
  - Infant of diabetic mother (born to mother with poorly controlled diabetes [type 1, type 2, or gestational]).
  - Erythroblastosis fetalis—alloimmune hemolytic disease of the newborn due to Rh or ABO incompatibility.
  - Polycythemia.
  - Sepsis.
  - Surreptitious insulin administration.

PERMANENT HYPERINSULINEMIA

- Most common variety is an autosomal recessive defect caused by mutation in the genes coding a component of K_{ATP} channel involved in glucose-regulated insulin release. The genes most commonly affected control the sulfonylurea receptor (SUR1) and the inward rectified potassium channel.

- Autosomal-dominant forms of hyperinsulinism are usually milder and caused by activating mutation in glucokinase (GCK) gene and glutamate dehydrogenase gene (GLUD1).
- Sporadic forms of hyperinsulinism can result in either focal or diffuse hyperplasia of β-cells. Focal adenomatous hyperplasia is caused by loss of the maternal allele from chromosome 11p15 and replacement with the paternal allele (paternal disomy).

Treatment

- Frequent feeding (feed q3–4h) to reduce frequency and severity of hypoglycemic events.
- IV glucose if necessary.
- In severe, prolonged cases treatment with diazoxide, somatostatin, and/or pancreatectomy may be necessary.

DISORDERS OF THYROID/ADRENALS

Hyperthyroidism

Definition

↑ synthesis and secretion of thyroid hormone.

JUVENILE GRAVES DISEASE

- Most common cause of hyperthyroidism in children and adolescents.
- Occurs more frequently in females (male-to-female ratio 1:5).
- Triad of:
    - Hyperthyroidism with diffuse goiter.
    - Ophthalmopathy (present in over one-half of the patients) with proptosis.
    - Dermopathy: Pretibial myxedema is present in 1–2% of adults; it rarely occurs in children.

Etiology

- Autoimmune disorder with antibodies against thyroid-stimulating hormone (TSH) receptor which is primarily expressed in the thyroid (thyrotropin receptor stimulating antibodies [TSHR-Ab] that activate the TSH receptor).
- This leads to inappropriate stimulation of the thyroid with subsequent gland enlargement and increased thyroid hormone production.

Signs and Symptoms

- Gradual onset (6–12 months).
- Emotional disturbance, change in academic performance.
- Insomnia.
- Palpitations.
- Fatigue, muscle weakness, ↑ sweating.
- ↑ appetite with ↓ or no weight gain.
- Goiter.
- Heat intolerance.
- Fine tremors.
- Exophthalmos.

EXAM TIP

Juvenile Graves disease causes 95% of thyrotoxicosis in children.

WARD TIP

Goiter is almost always present in hyperthyroidism and is usually symmetrical, smooth, soft, and nontender.

- Menstrual irregularities.
- **Thyroid storm:** Life-threatening condition that is characterized by:
    - Hyperpyrexia upto 104°F (40°C).
    - Severe tachycardia out of proportion to fever, leading to high-output cardiac failure.
    - Central nervous system (CNS) manifestations (agitation, delirium, psychosis, confusion, obtundation, coma, and convulsions).
    - Other symptoms include severe vomiting, diarrhea, abdominal pain.

LABORATORY FINDINGS

- Elevated total and free thyroxine (T_4) and total and free triiodothyronine (T_3) levels.
- ↓ TSH.
- Elevated TSHR-Ab.

TREATMENT OF HYPERTHYROIDISM

- Treatment depends on the age and severity of the disease and may include anti-thyroid medications, radioiodine ablation, or surgical thyroidectomy.
    - Anti-thyroid medication therapy is typically first-line treatment. Methimazole and propylthiouracil (PTU) have traditionally been used. PTU 5–10 mg/kg/day q8h PO or methimazole 0.25–1 mg/kg/day q8h. Side effects occur in 20–30% and include agranulocytosis, hepatotoxicity, urticaria, arthralgia, and very rarely vasculitis. The FDA placed a black box warning for PTU and is now no longer recommended as first-line treatment due to risk of severe hepatotoxicity making methimazole first line.
    - Radioactive iodine ablation use is increasing and is mostly for those who do not achieve remission or experience side effects with anti-thyroid medication, or in those >10 years. Often requires lifelong thyroid hormone replacement.
    - Surgery with thyroidectomy is very safe and effective immediately. Also requires lifelong thyroid hormone replacement.
- For thyroid storm, besides PTU or methimazole and beta-blocker to decreased adrenergic effects, can also give bile acid sequestrants, iodides (saturated solution of potassium iodide [SSKI] or Lugol's solution) every 6–8 hours and glucocorticoids. Both PTU and glucocorticoids inhibit the peripheral conversion of T_4 to T_3.

Hypothyroidism

DEFINITION

- ↓ production of thyroid hormone either from primary defect at the level of thyroid or secondary to hypothalamic pituitary disorder.
- In serum, 99.8% of T_4 and 99.7% of T_3 are bound to several serum proteins including thyroxine-binding protein. Only 0.02% of T_4 and 0.3% of T_3 are present as free fractions, which are biologically active (see Table 16-2).

CONGENITAL HYPOTHYROIDISM

Incidence is same worldwide (1 in 4000). Most common preventable cause of intellectual disability.

ETIOLOGY

- Sporadic: Majority of cases and most due to thyroid dysgenesis (absent thyroid, hypoplastic thyroid, ectopic thyroid).

TABLE 16-2. Thyroid Functions in Different Thyroid Conditions

	T$_4$	T$_3$	FT$_4$	FT$_3$	TSH	rT$_3$	T$_3$U
Primary hypothyroidism	L	L	L	L	H	L	L
Secondary hypothyroidism	L	L	L	L	N or L	L	L
Subclinical hypothyroidism	N	N	N	N	Slightly H	N	N
Subclinical hyperthyroidism	N	N	N	N	L	N	N
Euthyroid sick syndrome	L	L	L or N	L	N	H	L
TBG deficiency	L	L	N	N	N	N	H
TBG excess—TSH normal	H	H	N	N	H	N	L
Hypothyroxinemia of prematurity	L	L	L	L	N	L	L

H = high, L = low, N = normal.

FT$_3$, free triiodothyronine fraction; FT$_4$, free thyroxine fraction; rT$_3$, reverse T$_3$; T$_3$, triiodothyronine; T$_3$U, T$_3$ resin uptake; T$_4$, thyroxine; TBG, thyroxine-binding globulin.

- Iodine deficiency remains a major cause of transient congenital hypothyroidism worldwide. It resolves during the first few months or years of life.
- Prenatal exposure to radioiodine or antithyroid medications can also cause transient congenital hypothyroidism.
- Rarely hereditary: Thyroid dyshormonogenesis (defect in synthesis of thyroid hormone) and generalized thyroid hormone resistance.

SIGNS AND SYMPTOMS

- Most cases are asymptomatic at birth.
- Postmaturity, macrosomia.
- Wide fontanelle.
- Prolonged jaundice.
- Macroglossia and feeding problems.
- Hoarse cry.
- Abdominal distention, constipation.
- Umbilical hernia.
- Hypotonia or lethargy.
- Goiter (in some dyshormonogenesis).
- If left untreated:
  - Slowed development, late teeth, late milestones, short stature.
  - Eventual mental retardation.

DIAGNOSIS

Newborn screening:
- **Primary T$_4$–sequential TSH:**
  - Used by most North American programs.
  - Initial filter paper blood spot: T$_4$ with TSH measurement in specimens with low T$_4$ values.
  - Uses a percentile as the cutoff, with 10th percentile being the usual standard.
- **Primary TSH–sequential T$_4$:**
  - Used in all European countries (except the Netherlands), Japan, Australia, and parts of North America.

WARD TIP

Classic findings of congenital hypothyroidism are rare in the early neonatal period due to placental transfer of some maternal thyroid hormone (T4).

EXAM TIP

Early diagnosis of congenital hypothyroidism is crucial to prevent or minimize cognitive impairment. Ideally treatment should be initiated within the first 2 weeks of life.

- Initial TSH measurement, supplemented by T_4 in cases of high TSH.
- Cutoff point for recall is TSH 20–50 μU/mL with low T_4 (<5 μg/dL) or TSH >50 μIU/mL.

TREATMENT

- Oral levothyroxine is the only treatment of choice and should be initiated as early as possible at 10–15 μg/kg/day.

ACQUIRED HYPOTHYROIDISM

> A 10-year-old girl has a 3-year history of growth failure. A moderate-sized goiter is palpated. T_4 is 3.1 μg/dL, and TSH 322 μU/mL. *Think: Acquired hypothyroidism.*
> Congenital hypothyroidism is generally diagnosed in neonatal life because of newborn screening. Hypothyroidism that begins in childhood is usually Hashimoto disease. Initial signs and symptoms of hypothyroidism may be subtle. Growth retardation is usually not severe. However, if it remains unrecognized and untreated, linear growth is severely retarded and sexual maturation is also delayed. Goiter is the hallmark of classic Hashimoto disease. The results of the thyroid function test depend on stage of disease. TSH is elevated. Antithyroglobulin and anti–thyroid peroxidase (anti-TPO antibody) may be present. Iodine deficiency is one of the most common causes of acquired hypothyroidism worldwide.

- Prevalence in children is 0.15% with a female-to-male ratio of 3:1.
- Lymphocytic thyroiditis (Hashimoto) is the most common cause. It is an autoimmune disorder characterized by lymphocytic infiltration of thyroid and presence of:
  - Antithyroglobulin antibodies.
  - Anti–thyroid peroxidase (anti-TPO) antibodies.
- Other causes include thyroid surgery and irradiation, medications (iodine, lithium, amiodarone, etc.), pituitary or hypothalamic dysfunction (secondary or tertiary acquired hypothyroidism).

> **WARD TIP**
>
> Look for hypothyroidism in Down syndrome, Turner syndrome, type 1 diabetes mellitus, celiac disease, and Klinefelter syndrome.

SIGNS AND SYMPTOMS

- Goiter.
- Growth deceleration.
- Delayed skeletal maturation.
- Fatigue, lethargy.
- Constipation.
- Cold intolerance.
- Bradycardia.
- Dry skin.
- Weight gain.
- Delayed deep tendon reflexes.

TREATMENT

Levothyroxine 2–4 μg/kg/day.

Thyroid Neoplasm

EPIDEMIOLOGY

- Two percent of children have palpable thyroid nodules. Most are benign.
- Most common pediatric endocrine tumor (differentiated thyroid cancer–included papillary and follicular carcinoma).

- Family history (in medullary thyroid cancer seen with multiple endocrine neoplasia [MEN2]).
- Prior irradiation (in papillary thyroid cancer).

TYPES

- Benign thyroid adenomas: Follicular adenomas are the most common tumor (approximately 1% are toxic adenoma and cause hyperthyroidism).
- Thyroid carcinoma: Arise from:
  - Follicular epithelium:
    - Papillary carcinoma (most common; focal calcification [i.e., psammoma in 40–50%]).
    - Follicular carcinoma (higher prevalence in areas with iodine deficiency).
    - Insular carcinoma (poorly differentiated).
  - C cells: Medullary carcinoma (produce calcitonin). Associated with type 2 multiple endocrine neoplasia (MEN).

SIGNS AND SYMPTOMS

Solitary or multiple thyroid nodules (risk of malignancy in solitary nodules in children is 30–50%).

DIAGNOSIS

- Thyroid profile (thyroid functions are usually normal).
- Calcitonin (for medullary cancer).
- Thyroid ultrasound.
- Fine-needle aspiration.
- Definite diagnosis by surgical excision.

TREATMENT

- Papillary and follicular cancer:
  - Near total or total thyroidectomy (complications include bleeding, hypoparathyroidism, damage to recurrent laryngeal nerve) with modified neck dissection, if needed.
  - Postoperative ^{131}I ablation if the risk for recurrence is high.
  - Replacement thyroxine (higher doses in patients with ↑ risk of recurrence).
- Medullary thyroid cancer:
  - Total thyroidectomy.
  - Prophylactic thyroidectomy if positive for MEN mutation, before age 5 years in MEN 2A and in the first year of life with MEN 2B.

Congenital Adrenal Hyperplasia (CAH)

DEFINITION

- Genetic defect of adrenal corticosteroid and/or mineralocorticoid synthesis.
- ↓ in cortisol secretion results in a ↓ in negative feedback at the level of hypothalamus and pituitary gland.
- ↑ ACTH secretion results in markedly elevated production of the precursors before the block.

EPIDEMIOLOGY

- Most common cause of ambiguous genitalia.
- Incidence of classical 21-hydroxylase CAH is 1 in 15,000 live births.

WARD TIP

Cervical lymphadenopathy: Rapid and painless enlargement of a thyroid growth may suggest neoplasia.

EXAM TIP

Incidence of malignancy of a thyroid nodule is higher in children than in adults.

WARD TIP

A newborn with ambiguous genitalia is a medical and social emergency.

ETIOLOGY

- 21-hydroxylase deficiency (95% of all CAH):
    - Defect in conversion of 17- hydroxyprogesterone to 11-deoxycortisol.
    - Three-quarters of cases are salt wasters.
    - Ambiguous genitalia in the females (clitoral enlargement and a common urethral-vaginal orifice, normal uterus and ovaries); normal genitalia in males.
    - Milder form (nonclassical variant) has normal genitalia in females and presents late with premature pubarche.
- 11β-hydroxylase deficiency: HTN with low K frequently present because of excessive deoxycorticosterone (DOC).
- Ambiguous genitalia in females and precocious puberty in males.
- 3β-hydroxysteroid dehydrogenase:
    - Ambiguous genitalia in both sexes.
    - Salt wasting is present.
- 17-hydroxylase/17,20-lyase deficiency:
    - Normal genitalia in females; undervirilized or ambiguous genitalia in males.
    - Females may present with delayed puberty, primary amenorrhea, and lack of secondary sexual characteristics.
    - HTN with low K frequently present.
- Congenital lipoid adrenal hyperplasia:
    - Rare but most severe form of CAH.
    - Normal genitalia in females; undervirilized or ambiguous genitalia in males.
    - Salt wasting is present and severe.
    - All adrenal hormones and their precursors are low.

SIGNS AND SYMPTOMS

- Clinical features result from both the hormonal deficiencies (cortisol and aldosterone) and excessive production of precursors (17-hydroxyprogesterone, androstenedione, DOC).
- Female pseudohermaphroditsm: Ambiguous genitalia in female with normal 46,XX chromosome (21-hydroxylase, 11β-hydroxylase, 3β-hydroxysteroid dehydrogenase deficiency).
- Male pseudohermaphroditism: Ambiguous genitalia in male with 46,XY chromosome (3β-hydroxysteroid dehydrogenase, 17-hydroxylase/17,20-lyase deficiency, and congenital lipoid adrenal hyperplasia).
- Hypoglycemia (from cortisol deficiency).
- Salt wasting (21-hydroxylase, 3β-hydroxysteroid dehydrogenase, and congenital lipoid adrenal hyperplasia).
- HTN with hypokalemia (11β-hydroxylase and 17 hydroxylase/17,20-lyase deficiency).
- Vomiting, dehydration, and shock at 2–4 weeks of age.

DIAGNOSIS

- Newborn screening (elevated 17-hydroxyprogesterone level for 21-hydroxylase).
- Karyotype.
- Hyponatremia, hyperkalemia, hypochloremia, hypoglycemia.
- Markedly ↑ 17-hydroxyprogesterone for gestational age and weight (for 21-hydroxylase).
- Low baseline cortisol and low cortisol 60 minutes after 1–24 ACTH (Cortrosyn) stimulation.
- Elevated plasma renin activity (PRA).
- Genetic testing (DNA analysis for genetic mutations in the affected gene).
- Prenatal diagnosis (in pregnancy with ↑ risk).

WARD TIP

Combination of hyperkalemia and hyponatremia clue to diagnosis of classical CAH of salt-wasting variety.

WARD TIP

Most urgent tests for congenital adrenal hyperplasia:
1. Serum glucose
2. Serum electrolytes
Other tests: Cortisol, testosterone, 17-OH progesterone

TREATMENT

- Fluid and electrolyte replacement.
- Normal saline (NS) 20 mL/kg bolus, then maintenance plus ongoing fluid losses with D_5NS.
- Management of hypoglycemia.
- Stress dose of hydrocortisone (mineralocorticoid and glucocorticoid activity) 50–100 mg/m^2 IV bolus should be given initially, followed by 50–100 mg/m^2/24 hr for acute adrenal crisis. Once crisis is improved, switch to PO 10–15 mg/m^2/24 hr).
- Fludrocortisone (mineralocorticoid) 0.1–0.2 mg/day.
- Salt replacement (8–10 mEq/kg/day in the first few months of life, as Na content of formula and breast milk is quite low).
- Prenatal treatment: Treat mother with a pregnancy at risk for 21-hydroxylase deficiency, with dexamethasone.

Cushing Syndrome

DEFINITION

Characteristic pattern of obesity with or without HTN due to excessive glucocorticoid production/exposure.

ETIOLOGY

- Iatrogenic from exogenous corticosteroid (most common cause of hypercortisolism).
- Cushing disease: Bilateral adrenal hyperplasia due to excessive secretion of ACTH, usually by pituitary corticotroph adenoma. It is the most common cause of endogenous hypercortisolism in children.
- Cushing syndrome: Excess cortisol secretion by unilateral adrenocortical tumors (adenoma, carcinoma) or bilateral adrenal hyperplasia (primary pigmented micronodular adrenal hyperplasia).
- Ectopic ACTH syndrome: Malignant nonendocrine tumor, e.g., small cell lung carcinoma produces an excessive amount of ACTH. Extremely rare in children.

SIGNS AND SYMPTOMS

Truncal obesity, rounded moon facies, buffalo hump, purple striae, easy bruising, muscle weakness, osteopenia, statural growth retardation, acne, hirsutism, hyperpigmentation, HTN, hyperglycemia, depression, cognitive impairment.

DIAGNOSIS

- Elevated 24-hour urine test for free cortisol (UFC) and 17-hydroxycorticosteroid (17-OHS).
  - Mean rate of UFC in normal children is <70 mg/m^2/day.
  - Mean rate of 17-OHS is <7 mg/g of creatinine per day.
- 8:00 AM. ACTH and cortisol: Elevated ACTH level (>29 pg/mL with elevated UFC) suggests Cushing disease or ectopic ACTH production.
- Midnight plasma cortisol and ACTH (midnight cortisol >4.4 µg/dL is highly suggestive of Cushing but does not differentiate between Cushing syndrome versus Cushing disease).
- Low-dose dexamethasone suppression test:
  - Overnight dose 0.03 mg/kg (max 1 mg) at 11 PM X1 dose *or*
  - 0.03 mg/kg/day (max 0.5 q6h) for 2 days.
  - Normal if suppression results in plasma cortisol of <5 µg/dL.
  - Nonsuppression with elevated UFC suggests the diagnosis of Cushing but does not differentiate between Cushing syndrome versus Cushing disease.

WARD TIP

In CAH, blood should be drawn for steroid profile before the administration of hydrocortisone.

EXAM TIP

Cushing disease is a state of hypercortisolism secondary to adrenocorticotropic hormone (ACTH)-producing pituitary adenoma.

WARD TIP

Cushing syndrome occurs when the body produces excess cortisol. Cushing disease occurs when a tumor on the pituitary produces excess ACTH.

- High-dose dexamethasone suppression test:
    - Overnight dose of 0.12 mg/kg/day (max 8 mg) *or*
    - 0.12 mg/kg/day (max 2 mg q6h) for 2 days.
    - Suppression (cortisol <5 μg/dL) suggests Cushing disease, while non-suppression suggests Cushing syndrome.
    - 24 UFC paradoxically rises in primary pigmented nodular adrenal disease after high-dose dexamethasone suppression test.
- Ovine corticotropin-releasing hormone (CRH) stimulation test/bilateral petrosal sinus sampling: ↑ in ACTH after IV CRH suggests Cushing disease.
- Polycythemia, lymphopenia, and eosinopenia can be associated findings.
- Abdominal computed tomography (CT) (adrenal tumors).
- Pituitary magnetic resonance imaging (MRI) (pituitary adenoma).

DIFFERENTIAL DIAGNOSIS

- Exogenous obesity (pseudo-Cushing state).
- Normal growth rate.
- Cortisol level suppressed by dexamethasone.

TREATMENT

- Pediatric endocrine, surgical, and neurosurgical consultation.
- Adrenalectomy (unilateral or bilateral for adrenal tumors or bilateral nodular hyperplasia, respectively).
- Chemotherapy with mitotane for adrenal cancer with metastasis (after surgery).
- Transsphenoidal resection of pituitary adenoma.
- Fractionated radiotherapy for recurrent pituitary adenoma.

Adrenal Insufficiency

DEFINITION

- Adrenal cortex fails to produce enough glucocorticoid to mount response to stress.
- May be primary adrenal disorder or secondary to ACTH deficiency/resistance.
- Mineralocorticoid deficiency is present in primary adrenal disorder but is not part of secondary adrenal insufficiency, as aldosterone secretion depends on renin/angiotensin system.

ETIOLOGY

Primary Adrenal Insufficiency (Low Cortisol/Elevated ACTH)
- **Congenital:**
    - CAH.
    - Congenital adrenal hypoplasia (X-linked).
    - ACTH resistance.
    - Adrenal leukodystrophy (X-linked-recessive disorder of metabolism of very long chain fatty acids).
- **Acquired (Addison disease):**
    - Autoimmune destruction (80%).
    - Tuberculosis (TB).
    - Bilateral adrenal hemorrhages (meningococcal septicemia).

- AIDS (opportunistic infections).
- Antiphospholipid antibody syndrome.

Secondary Adrenal Insufficiency (Low Cortisol/Low ACTH)
- **Congenital:**
  - Congenital hypopituitarism.
  - Septo-optic dysplasia.
- **Acquired:**
  - Iatrogenic: Adrenal insufficiency from abrupt discontinuation of glucocorticoids after prolonged use.
  - Pituitary or hypothalamic tumors.

SIGNS AND SYMPTOMS

- Weakness, fatigue, anorexia, nausea, vomiting, weight loss.
- Postural hypotension (more marked in primary adrenal insufficiency).
- Hyperpigmentation of skin and mucosal surfaces (in primary adrenal insufficiency due to elevated ACTH/melanocyte-stimulating hormone [MSH]).
- Salt craving (in primary adrenal insufficiency).
- Adrenal crisis (fever, vomiting, dehydration, and shock precipitated by infection, trauma, or surgery in susceptible patient).

DIAGNOSIS

- Hyponatremia, hyperkalemia, acidosis, hypoglycemia.
- AM plasma cortisol and ACTH level:
  - AM plasma cortisol <3 μg/dL is indicative of adrenal insufficiency while value >19 μg/dL makes it unlikely.
  - Basal plasma ACTH level invariably exceeds 100 pg/mL in primary adrenal insufficiency, while normal ACTH level does not rule out secondary adrenal insufficiency.
- Antiadrenal antibodies (in autoimmune destruction of adrenal glands).
- ACTH stimulation test:
  - 1–24 ACTH (Cortrosyn) given IV or IM and cortisol level measured at baseline and 30–60 minutes after the injection.
  - For primary and severe/prolonged adrenal insufficiency use 250 μg Cortrosyn.
  - For secondary adrenal insufficiency that is mild or recent onset use 1 μg.
  - Normal response is plasma cortisol concentration of 18–20 μg/dL at 30–60 minutes post Cortrosyn.
- CT scan of adrenal glands (in primary adrenal insufficiency).
- MRI of the pituitary gland and hypothalamus (in secondary adrenal insufficiency).

TREATMENT

- Hydrocortisone (10–24 mg/m^2/24 hr divided in 2–3 doses). Double or triple the oral dose of glucocorticoids for febrile illness or injury.
- Fludrocortisone (0.05–0.2 mg PO daily).
- In acute adrenal insufficiency (adrenal crisis):
  - Volume replacement.
  - Hydrocortisone 50 mg/m^2 IV, then 50–100 mg/m^2/24 hr or methylprednisolone 7.5 mg/m^2/24 hr.
  - Switched to oral therapy in 2–3 days.

Pheochromocytoma

DEFINITION

- Catecholamine-producing tumor of chromaffin tissue of adrenal medulla (80–85% of cases).
- Catecholamine-producing tumors of extra-adrenal origin are called paragliomas (15–20% of cases).
- Usually benign, well encapsulated (<10% malignant).
- In children: Frequently familial, bilateral, and multifocal.
- Recurrent tumor may appear years after initial diagnosis.

ETIOLOGY

- May occur in isolation (sporadic).
- Also seen in the MEN 2 (bilateral), von Hippel–Lindau, neurofibromatosis type 1, and familial carotid body tumor syndromes.

SIGNS AND SYMPTOMS

- Nonspecific symptoms.
- Headache, palpitations, ↑ sweating, anxiety.
- Nausea, vomiting, weight loss, tremor, fatigue, chest or abdominal pain, and flushing.
- Sustained HTN (in children).
- Hyperglycemia.
- Epinephrine-producing tumor may present with postural/orthostatic hypotension.

DIAGNOSIS

- Plasma-free metanephrines (metanephrine and normetanephrine): Unequivocally elevated, four to five times the upper limit of the reference range.
- ↑ urinary catecholamines or metabolites (24-hour urinary excretion of fractionated metanephrines), vanillylmandelic acid (VMA).
- Serum chromogranin A.
- Abdominal ultrasound (US).
- Abdominal CT and MRI.
- ^{123}I MIBG (metaiodobenzylguanidine) scan.
- FDG PET (fluorodeoxyglucose positron emission tomography) scan.
- Octreoscan.

DIFFERENTIAL DIAGNOSIS

- Ganglioneuroma.
- Neuroblastoma.
- Ganglioneuroblastoma.

TREATMENT

- Surgical excision.
- Preoperative α_1 and α_2 adrenoreceptor blockade (phenoxybenzamine) and β adrenoreceptor blockade (propranolol, atenolol) are required to prevent hypertensive crisis and arrhythmias, respectively.
- Yearly follow-up evaluation for assessment of recurrence for at least 5 years (indefinitely in children with familial pheochromocytoma).

EXAM TIP

Tumors arising in the adrenal medulla produce both epinephrine and norepinephrine. Extra-adrenal tumors produce only norepinephrine.

EXAM TIP

Siblings of a patient with a pheochromocytoma should be periodically evaluated because of ↑ familial incidence.

WARD TIP

The most useful screening test for pheochromocytoma is blood pressure.

WARD TIP

Increased urinary norepinephrine indicates an extra-adrenal site of a pheochromocytoma, whereas increased epinephrine indicates an adrenal lesion.

WARD TIP

After successful surgery of a pheochromocytoma, catecholamine excretion returns to normal in about 1 week.

DISORDERS OF CALCIUM AND BONE METABOLISM

Hyperparathyroidism

A 10-year-old girl has severe abdominal pain and gross hematuria. She passes a calculus in her urine. She had received no medication and has no family history of renal stones. *Think: Primary hyperparathyroidism.*

Symptoms of primary hyperparathyroidism include painful BONES, renal STONES, abdominal pain (GROANS), and psychiatric MOANS (poor concentration, depression, fatigue). It is a common cause of hypercalcemia. Hypercalcemia in the presence of elevated serum parathyroid hormone level confirms the diagnosis of primary hyperparathyroidism. Other biochemical findings include hypercalciuria and hypophosphatemia.

DEFINITION

Hypercalcemia accompanied by increased or inappropriately normal parathyroid hormone (PTH) level.

EPIDEMIOLOGY

Uncommon in children.

ETIOLOGY

- Primary (defect of parathyroid gland):
    - Parathyroid adenoma—most common cause of primary hyperparathyroidism.
    - Generalized hyperplasia of all glands (MEN 1 and MEN 2A).
    - Parathyroid carcinoma.
- Secondary (response to hypocalcemia):
    - Chronic renal failure (CRF).
    - Renal tubular acidosis.
    - Vitamin D–deficiency rickets.
    - Treatment (with phosphorus) for hypophosphatemic rickets.
    - Liver failure.
- Tertiary hyperparathyroidism: Adenomatous change in parathyroid in the setting of CRF leading to overexcretion of PTH and subsequent hypercalcemia.

SIGNS AND SYMPTOMS

- Clinical manifestation of hypercalcemia.
- Muscle weakness, anorexia, nausea, vomiting, constipation, polyuria, dehydration, failure to thrive, coma, seizures, fever, renal stones.

DIAGNOSIS

- ↑ serum Ca.
- ↓ serum phosphorus.
- ↑ urinary calcium.
- ↑ PTH.
- Shortened QTc interval.
- Subperiosteal resorption seen with radiographs of the hands (with prolonged hyperparathyroidism).
- ^{99m}Tc-sestamibi scanning for parathyroid adenoma.

TREATMENT

- Hypercalcemia:
    - Hydration (IV NS at two to three times maintenance).
    - Furosemide 1 mg/kg q6h (↑ Na and Ca excretion).
    - Glucocorticoids (↓ intestinal absorption of Ca).
    - Calcitonin 4 U/kg SQ q12h.
    - Bisphosphonates (inhibit osteoclast mediated bone resorption and subsequent hypercalcemia).
    - Calcimimetics suppress PTH secretion in affected gland. Dialysis as a last resort.
- Primary hyperparathyroidism:
    - Resection of isolated adenoma.
    - For generalized hyperplasia resection of 3½ glands.
    - Vitamin D and calcium for postop hypocalcemia, which can be severe and prolonged due to hungry bone syndrome (hypocalcemia, hypophosphatemia, hypomagnesemia, and hyperkalemia) in cases of severe hyperparathyroidism.
- Secondary hyperparathyroidism: Treatment of the underlying cause.

Hypoparathyroidism

DEFINITION

- Decreased PTH from defective synthesis or secretion.
- Can lead to hypocalcemia and increased serum phosphate levels.

ETIOLOGY

- Autoimmune.
- Post-surgical after thyroid, parathyroid, or radical neck surgery for cancer.
- Familial: Autosomal dominant, autosomal recessive, and X-linked recessive.
- DiGeorge/velocardiofacial syndrome (deletion of chromosome 22q.11.2).
- Acute illness (PTH secretion is impaired in critical illness).
- Severe hypomagnesemia (usually <1 mg/dL).

SIGNS AND SYMPTOMS

- Most common presentation is numbness, tingling, paresthesia, muscle cramps.
- In severe cases, seizure, tetany, and mental status changes.
- In older asymptomatic patients, hyperreflexia, Chvostek's (facial twitching), and Trousseau's (carpopedal spasm) signs can be elicited.
- EKG may reveal prolongation of the QTc interval leading to arrhythmias.

DIAGNOSIS

- ↓ serum total Ca and ionized Ca.
- ↑ serum phosphate.
- Markedly ↓ PTH.
- Prolonged QTc interval.
- Total Ca ↓ by 0.8 mg/dL for each 1 g/dL ↓ in albumin below 4 g/dL.
- ↑ or ↓ in pH by 0.1 units ↓ and ↑ ionized Ca by 0.03 mmol/L, respectively.

DIFFERENTIAL DIAGNOSIS

Pseudohypoparathyroidism (PTH unresponsiveness). Markedly ↑ PTH.

TREATMENT

- Correct hypocalcemia:
    - Intravenous (IV) 10% calcium gluconate 2 cc/kg gradually over 10 minutes for acute symptomatic hypocalcemia.
    - To maintain normocalcemia: Continuous IV infusion (20–80 mg Ca/kg/24 hr).
    - Transition to PO calcium as soon as possible (25–100 mg Ca/kg/day).
- Correct hypomagnesemia.
- Vitamin D (calcitriol).

Metabolic Bone Disease

- **Osteopenia:** Deficiency in bone mass relative to age, sex, and race norms.
- **Osteoporosis:** Loss of bone mineral and matrix due to disproportionately low osteoblastic activity.
- **Osteomalacia:** Defective mineralization of the bone matrix.
- **Rickets:** Defective mineralization at the growth plate.

CLASSIFICATION OF RICKETS

Calcipenic

ETIOLOGY

- Nutritional:
    - Vitamin D deficiency.
    - Calcium deficiency.
- Genetic:
    - Vitamin D–dependent rickets type 1 (1α-hydroxylase deficiency causing defect in the conversion of 25(OH) vitamin D to 1,25(OH)$_2$ vitamin D).
    - Vitamin D–dependent rickets type 2 (mutation in the gene coding the vitamin D receptor causing hereditary vitamin D resistance).
- Drugs:
    - Corticosteroids.
    - Anticonvulsants.
- Prematurity.

Phosphopenic

- Genetic:
    - X-linked hypophosphatemic rickets (mutation in the *PHEX* gene).
    - Autosomal-dominant hereditary hypophosphatemic rickets (mutation in the gene for fibroblast growth factor 23).
    - Autosomal-recessive hereditary hyperphosphatemic rickets with hypercalciuria (mutation in the gene for renal sodium phosphate cotransporter NaP(i)-IIc).
- Tumor-induced hypophosphatemia (small, typically benign tumor mostly of mesenchymal origin).
- Dietary:
    - Intestinal malabsorption.
    - Breast-fed premature infants.
- Fanconi syndrome (renal loss of glucose, phosphate, amino acids, and bicarbonate).

CLINICAL FEATURES

- Genu varum (bow-legged deformity) during early childhood.
- Genu valgum (knocked-knee deformity) in older children.

> **EXAM TIP**
>
> Excluding those with chronic malabsorption syndromes or end-stage renal disease, most cases of rickets occur in dark-skinned breast-fed infants who have not received any vitamin D supplementation.

- Enlargement of wrists and knees.
- Rachitic rosary (enlargement of costochondral junctions).
- Harrison grooves (groove extending laterally from xiphoid process, corresponds to the diaphragmatic attachment).
- Frontal bossing.
- Craniotabes (generalized softening of calvaria).
- Bone pain.
- Proximal muscle weakness.

RADIOLOGICAL FEATURES

- Widening of epiphyseal plates.
- Cupping, splaying, and formation of cortical spurs.
- Deformities in shaft of long bones.

DIAGNOSIS

- Serum calcium, phosphorous, alkaline phosphatase level:
  - Alkaline phosphatase is elevated in most cases of rickets. Elevation is marked in calcium and vitamin D deficiency and mild in hypophosphatemic rickets.
  - Serum calcium and phosphorus tend to be low or low normal in all form of calcipenic rickets. Serum PTH is considerably elevated.
  - Low serum phosphate with normal calcium level suggests the diagnosis of hypophosphatemic rickets.
- 25(OH) vitamin D and 1,25(OH)$_2$ vitamin D level:
  - Low 25(OH) vitamin D is seen in all forms of vitamin D deficiency.
  - Normal 25(OH) vitamin D level with low 1,25(OH)$_2$ vitamin D level point to 1α-hydroxylase deficiency.
  - 1,25(OH)$_2$ vitamin D level is elevated in hereditary vitamin D resistance.
  - 1,25(OH)$_2$ vitamin D level is inappropriately normal in the setting of hypophosphatemia in X-linked and autosomal-dominant hypophosphatemic rickets.
- PTH level:
  - Moderate to severe hyperparathyroidism is characteristic of calcipenic rickets.
  - In hypophosphatemic rickets, PTH level may be normal or modestly elevated.
- Tubular reabsorption of phosphorous (TRP).

$$[1\text{-}\{(\text{Urine P} \times \text{Serum creatinine}) / (\text{Serum P} \times \text{Urine creatinine})\}] \times 100$$

  - Normal TRP value 85–95% for children.
  - A normogram is used to determine the renal tubular threshold maximum for phosphate as expressed per glomerular filtration rate (TMP/GFR).
  - Low TMP/GFR in the setting of low serum phosphate confirms inappropriate renal loses, characteristic of hypophosphatemic rickets.

TREATMENT

- **Nutritional rickets:**
  - 5000–15,000 IU of vitamin D PO for 4 weeks.
  - 600,000 IU in a single dose PO/IM for noncompliance (stoss therapy).
  - Ensure adequate calcium intake (350–1500 mg elemental calcium per day for 6 months).
- **1α-hydroxylase deficiency rickets:**
  - 1,25(OH)$_2$ vitamin D (calcitriol) 0.5–3 μg/day.
  - Adequate dietary calcium intake.

- **Hereditary vitamin D resistance:**
    - High doses of 1,25(OH)$_2$ vitamin D.
    - IV calcium in patients who do not respond to vitamin D.
- **Hypophosphatemic rickets:**
    - Phosphate (250–1000 mg elemental phosphorus in 2–3 divided doses).
    - 1,25(OH)$_2$ vitamin D is important for successful outcome. It enhances calcium and phosphate absorption and dampens phosphate stimulated PTH secretion.

NEUROENDOCRINE DISORDERS

Diabetes Insipidus (DI)

DEFINITION

Inability of kidneys to concentrate urine.

ETIOLOGY

- **Central** (↓ ADH production):
    - Congenital hypothalamic/pituitary defects (septo-optic dysplasia, holoprosencephaly).
    - Idiopathic, accidental or surgical trauma, infections (meningitis).
    - Neoplasms (suprasellar tumors).
    - Infiltrative and autoimmune diseases (histiocytosis X).
    - Drugs (ethanol, phenytoin).
- **Nephrogenic** (renal unresponsiveness to ADH):
    - X-linked recessive (vasopressin type 2 receptor mutation): Males—present in early infancy. Carrier females are asymptomatic.
    - Autosomal recessive or autosomal dominant (mutation in the renal water channel—aquaporin-2).
    - Idiopathic.
    - Renal diseases.
    - Hypercalcemia.
    - Hypokalemia.
    - Drugs (lithium, demeclocycline).

SIGNS AND SYMPTOMS

- **Central:**
    - Polyuria (>1.5 L/m^2/day).
    - Polydipsia (excessive thirst).
    - Enuresis.
    - Hypernatremic dehydration.
- **Nephrogenic:**
    - Polyuria, nocturia, failure to thrive (FTT), hyperpyrexia, vomiting.
    - Hypernatremic dehydration.

DIAGNOSIS

- ↑ serum osmolality (normal: <290 mOsm/kg).
- ↑ serum Na (normal: <145 mmol/L).
- ↓ urine osmolality.
- Water deprivation test to differentiate central DI from primary polydipsia: Withhold fluids for 8–10 hours (may need to be done in hospital). Serum osmolality >300 mOsm/kg with urine osmolality <600 mOsm/kg or plasma sodium >145 mEq/L establishes the diagnosis.

WARD TIP

In diabetes insipidus, there is high urine output despite significant dehydration.

- Once diagnosis is established, give pitressin (desmopressin/ADH).
  - Urine volume falls and osmolality doubles—central DI.
  - Less than twofold rise in urine osmolality—nephrogenic DI.
- Plasma vasopressin (low in central DI and high in nephrogenic DI).
- MRI: Posterior pituitary bright spot is diminished or absent in both forms of DI.

TREATMENT

- **Central:**
  - Fluids (3–4 L/m^2/day without vasopressin, 1 L/m^2/day with vasopressin).
  - Vasopressin (desmopressin [DDAVP]) 0.05–1.2 mg bid orally, 5–40 μg intranasally divided qd-bid, or 0.08 μg/kg subcutaneously divided q12).
- **Nephrogenic:**
  - Fluids.
  - Thiazide diuretic (promotes Na excretion in the distal tubule and alters inner medullary osmolality → ↑ proximal tubular reabsorption of Na and ↑ free water reabsorption from the collecting duct).
  - NSAIDs (nonsteroidal anti-inflammatory drugs): Indomethacin 2 mg/kg/day further enhances proximal tubular sodium and water reabsorption.

Syndrome of Inappropriate Secretion of Antidiuretic Hormone (SIADH)

DEFINITION

Hyponatremia with ↑ ADH and impaired water excretion.

ETIOLOGY

- Can be hereditary.
- Any CNS disorder: Encephalitis/meningitis.
- Brain tumor.
- Head trauma, intracranial bleeding.
- Psychiatric diseases.
- Postictal period.
- Positive pressure ventilation.
- Rocky Mountain spotted fever.
- Pneumonia.
- AIDS.
- Drugs (carbamazepine, chlorpropamide, vincristine, tricyclic antidepressant).

SIGNS AND SYMPTOMS

- Asymptomatic until Na < 120.
- Headache, nausea, vomiting, irritability, seizure.
- ↓ urine output.

DIAGNOSIS

- Hyponatremia (Na < 135 mmol/L).
- ↓ serum osmolality (<275 mOsm/kg).
- ↑ urine osmolality (>100 mOsm/kg).
- ↑ urine Na (usually >80 mEq/L).
- Low serum uric acid level.
- Normal renal, adrenal, and thyroid function.

WARD TIP

In SIADH, there is an absence of edema and dehydration.

WARD TIP

Urine osmolality <100 mOsm/kg excludes diagnosis of SIADH.

TREATMENT

- Treat the underlying disease.
- **Symptomatic with hyponatremia:** Hypertonic (3%) saline 6 mL/kg bolus ↑ Na by 5 mmol/L. Repeat bolus until patient stops seizing.
- **Asymptomatic:**
    - Fluid restriction (1000 mL/m^2/day).
    - Demeclocycline and lithium act on the collecting tubule to diminish responsiveness to ADH, thereby increasing water excretion.
    - Selective V2 receptor antagonist (tolvaptan)—cause selective water diuresis without affecting sodium and potassium excretion.
    - Oral urea (0.1–2.0 g/kg/day divided q6h) at low doses reduces natriuresis and at higher doses causes osmotic diuresis.

Cerebral Salt Wasting (CSW)

DEFINITION

Renal loss of Na during intracranial disease especially with subarachnoid hemorrhage.

Characterized by hyponatremia and extracellular fluid depletion due to inappropriate sodium wasting in the urine.

ETIOLOGY

High atrial natriuretic peptide (ANP) → natriuresis and diuresis (due to decreased sodium reabsorption and inhibition of renin release).

SIGNS AND SYMPTOMS

- Acute, intermittent excessive fluid and salt loss.
- ↑ urine output.
- Onset within first week of CNS insult.
- Duration variable usually lasts 2–4 weeks.
- Dehydration (↓ extracellular fluid).

DIAGNOSIS

- Hyponatremia (Na < 130 mmol/L) and low plasma osmolality.
- Inappropriately elevated urine osmolality that is isotonic with plasma.
- ↑ urine Na (usually > 40 mEq/L).
- See Table 16-3 for comparison between DI, SIADH, and CSW.

TREATMENT

- Water and salt replacement (0.9 or 3% NS).
- Long-term treatment is not needed as this disease process is transient and resolves within 2–4 weeks.

Hyperpituitarism

GIGANTISM/ACROMEGALY

- ↑ GH.
- If occurs before epiphyses close, → gigantism.
- If after epiphyses close, → acromegaly.

TABLE 16-3. Comparison Between SIADH and CSW

	SIADH	CSW
Body weight	↑	↓
Plasma volume	↑	↓
Serum Na	↓	↓
Serum osmolality	↓	↓
Urine osmolality	Higher than plasma	Isotonic with plasma
Urine flow rate	↓	↑
Plasma renin	↓	↓
Plasma aldosterone	↑	↓
Plasma ADH	↑	↓
Plasma ANP	↑	↑
Serum uric acid	↓	Normal

ADH, antidiuretic hormone; ANP, atrial natriuretic peptide; CSW, cerebral salt wasting; SIADH, syndrome of inappropriate secretion of antidiuretic hormone.

ETIOLOGY

- Pituitary gigantism is rare. Can occur at any age and has been observed as early as six months' age. Typically is a sporadic and isolated condition.
- Most commonly caused by growth hormone (GH)–secreting adenoma.
- Also seen with McCune Albright syndrome, MEN1, and Carney complex.

CLINICAL FEATURES

- Accelerated rate of linear growth and rapid weight gain.
- Coarsening of facial features (macrocephaly, frontal bossing) and mandibular prominence.
- Enlargement of hands and feet.
- Excessive sweating.
- GH-secreting adenomas are often associated with amenorrhea with or without galactorrhea in girls and symptoms of tumor compression in boys.

DIAGNOSIS

- Elevated insulin-like growth factor 1 (IGF-1) and IGF-binding protein 3 (IGFBP-3).
- GH may be normal or elevated.
- GH suppression test is gold standard for making definitive diagnosis if GH is elevated.
  - Measures serum GH response to an oral glucose load.
  - In normal individuals GH concentration falls below 1 ng/mL within 2 hours of the glucose load.
  - GH not suppressed by glucose in pituitary gigantism.
- MRI of the pituitary.

TREATMENT

- Transsphenoidal resection of adenoma.
- Somatostatin and dopamine agonist (bromocriptine) for incomplete resection.

Prolactin Excess

ETIOLOGY

- Prolactin-secreting adenoma: Microadenoma (<1 cm) or macroadenoma (>1 cm).
- Tumors that disrupt pituitary stalk preventing inhibitory control.
- Drugs (phenothiazines, risperidone, metoclopramide, estrogen, cocaine).
- Hypothyroidism.
- Liver or renal failure.
- Macroprolactinemia (variant molecule).
- Physical stress.

CLINICAL FEATURES

- Galactorrhea.
- Menstrual irregularities/amenorrhea.
- Decreased libido.
- Gynecomastia.

DIAGNOSIS

- Elevated prolactin level (>20 ng/mL).
- MRI (hypothalamic-pituitary region).

TREATMENT

- Treatment of the cause.
- Dopamine agonists (bromocriptine, cabergoline) are the first line of treatment.
- Transsphenoidal surgery if medical treatment is unsuccessful.

> **WARD TIP**
>
> Prolactin secretion is inhibited by dopamine in pituitary prolactinomas. Therefore, treatment includes dopamine agonists such as bromocriptine.

Hypopituitarism

> An infant has hypoglycemia and a micropenis. *Think: Hypopituitarism.*
> Hypopituitarism—growth hormone deficiency + deficiencies of other pituitary hormones. Severe hypoglycemia may be an initial presentation. Most infants present in the first few days of life with severe hypoglycemia. In males, microphallus is important diagnostic information. It is due to LH deficiency as LH stimulates testosterone production from testes during the last trimester of pregnancy causing lengthening of penis. Prolonged jaundice may be present which is due to associated central (hypothalamic or pituitary) hypothyroidism. Children who remain unrecognized may present later with failure to thrive and poor weight gain.

DEFINITION

Deficiency of more than one pituitary hormone.

PHYSIOLOGY

- ACTH deficiency → decreased adrenal glucocorticoids (cortisol) → fatigue, anorexia, weight loss, hypoglycemia, eosinophilia. In severe cases, it can lead to cardiovascular collapse, shock, and death.

- TSH deficiency → decreased thyroid hormone → fatigue, cold intolerance, decreased appetite, dry skin, bradycardia.
- Luteinizing hormone (LH) and follicle-stimulating hormone (FSH) deficiency → gonadal hypofunction. In females it causes decreased estradiol and can lead to premature ovarian failure. Can also cause irregular menses or amenorrhea and hot flashes. In males it causes decreased testosterone secretion → micropenis. Patients may also present with delayed puberty.
- Prolactin deficiency → only known clinical manifestation is inability to lactate.
- GH deficiency → presents with short stature and delayed growth.
- Antidiuretic hormone (ADH) deficiency → central diabetes insipidus presenting with polyuria, nocturia, polydipsia, and hypernatremia.

ETIOLOGY

- **Congenital:**
  - Inherited (mutation in the gene encoding pituitary transcription factor Pit-1).
  - Sporadic developmental defects: Midline anomalies (septo-optic dysplasia, cleft palate), holoprosencephaly.
- **Acquired:**
  - Tumors and their treatment (craniopharyngioma).
  - Head trauma.
  - CNS irradiation.
  - Histiocytosis X.
  - Autoimmune hypophysitis.
  - Hemochromatosis.
  - Perinatal asphyxia
  - Disseminated tuberculosis or sarcoidosis.

SIGNS AND SYMPTOMS

- Depends on missing hormone and/or etiological cause.
- Visual and neurologic complaints.

TREATMENT

Replacement directed toward the hormonal deficiency.

GROWTH DISORDERS

Short Stature

DEFINITION

Height below the 2.5th percentile for age and gender: (>2 standard deviations below the mean).

Intrauterine Growth Retardation

- Chronological age (CA) = Bone age (BA) = Height age (HA).
- Normal growth velocity depends on age and pubertal stage:
  - First 2 years of life (infantile phase): Linear growth is initially very rapid and gradually decreases. Overall growth in this phase is about 30–35 cm.
  - Age 2–4 years: 5.5 to 9 cm/yr

- Age 4–6 years: 5 to 8.5 cm/yr
- Age 6 years to puberty: 4–6 cm/yr
- During puberty (girls Tanner II–III): 8 to 14 cm/yr
- During puberty (boys Tanner IV): 8 to 14 cm/yr

Genetic Potential: Midparental Height
- For males: Add 5 inches to mother's height and average it with father's height.
- For females: Subtract 5 inches from father's height and average it with mother's height.

Familial (Genetic Short Stature)
- Common cause of short stature.
- Height is within family norm (usually at least one parent has short stature).
- Normal rate of growth (follow steady channel after 2–3 years).
- Normal bone age.
- Puberty at average age.

> **EXAM TIP**
>
> The most common causes of short stature are normal variants including familial short stature and constitutional delay.

Constitutional Delay
- Most common cause of short stature.
- Normal variant of growth.
- Normal at birth, then growth decelerates during first 2 years of life.
- Both length and weight gain decelerate until age 2–3 years.
- Resume growth rate by 3–4 years paralleling a lower percentile curve.
- Delayed puberty (second growth deceleration at age 12–14 years).
- Described as "late bloomers" because of catch-up growth when they do enter puberty.
- Delayed bone age (bone age = height age but ≠ to chronological age).

> **EXAM TIP**
>
> Children with constitutional delay are the so-called "late bloomers."

Nutritional
- Inflammatory bowel disease.
- Celiac disease.
- HIV infection.
- Other conditions causing malnutrition.

Psychosocial Deprivation
Children with psychosocial deprivation clinically resemble children with GH deficiency with retardation of bone age and similar findings on GH stimulation testing; however, testing and growth revert to normal when the child is removed from the deprived environment.

Small for Gestational Age (SGA)
- Birth weight and length <10th percentile for gestational age.
- Most SGA infants catch up by 2 years of age.

Glucocorticoid Therapy
Effects are dose related.

Intrauterine Growth Retardation
- Pathologically growth-restricted infants.
- Rheumatologic and renal disease (CKD, renal tubular acidosis).
- Pulmonary disease (cystic fibrosis).

GROWTH HORMONE DEFICIENCY (GHD)

- Pathologic cause of short stature.
- Hypoglycemia and micropenis (especially if associated with hypopituitarism).

- Height below genetic potential.
- ↓ growth velocity (<25th percentile for age).
- Downward crossing of percentiles on growth chart after age 2–3 years.
- ↓ muscle mass, ↑ fat mass.
- Pubertal delay.
- Causes—idiopathic, hereditary, hypothalamic/pituitary malformation, hypothalamic/pituitary tumor, head trauma, CNS surgery, CNS radiation, meningitis/encephalitis, autoimmune hypophysitis, histiocytosis X, sarcoidosis, and hemochromatosis.

DIAGNOSIS

- Delayed bone age.
- Low IGF-1, low IGFBP-3 (insulin-like growth factor-binding protein 3), inadequate response to GH stimulation.

TREATMENT

Biosynthetic human GH.

GROWTH HORMONE INSENSITIVITY (LARON SYNDROME)

- Features similar to GHD.
- GH receptor defect.
- Normal or elevated GH level.
- Low IGF-1, IGF-2, and IGFBP-3.
- Absent or low growth hormone binding protein (GHBP).

TREATMENT

Biosynthetic IGF-1.

HYPOTHYROIDISM

- Pathologic cause of short stature.
- ↓ growth velocity.
- Delayed bone age.

DIAGNOSIS

Elevated TSH, decreased free T_4 with primary hypothyroidism.

Low TSH and low T_4 with central hypothyroidism.

TREATMENT

Levothyroxine (T_4).

CUSHING SYNDROME

- Pathologic cause of short stature.
- ↑ cortisol inhibits growth, and delays bone age.
- Abnormal weight gain.
- Truncal obesity, rounded moon facies, buffalo hump, purple striae.

ETIOLOGY

Endogenous or exogenous steroids.

DIAGNOSIS

Elevated 24-hour urine test for free cortisol is the best screening test.

TREATMENT

Treat the cause.

CHROMOSOMAL DISORDERS

- Turner syndrome (45X).
- Down syndrome (trisomy 21).
- Silver-Russell syndrome.
- Prader-Willi syndrome.

Tall Stature

DEFINITION

Height more than 2 standard deviations above the mean for age and gender.

Familial or Constitutional Tall Stature
- Most common.
- Family history of tall stature.
- Lack of any dysmorphic features.
- Normal bone age.

Hormonal
- GH excess → gigantism or acromegaly.
- Early/Precocious puberty: ↑ sex steroids (tall as child, short as adult from early epiphyseal closure).
- CAH: ↑ adrenal androgens (tall as child, short as adult from early epiphyseal closure).
- Hyperinsulinism/obesity.
- Hypogonadotropic hypogonadism (Kallmann syndrome).

Syndromes
- Marfan syndrome (autosomal dominant connective tissue disorder).
- Homocystinuria (inherited inborn error of metabolism).
- Klinefelter syndrome (47XXY).
- Sotos syndrome (not truly endocrine, associated mental retardation)—cerebral gigantism: neonates are large for gestational age and continue to grow rapidly during early years of childhood.
- Beckwith-Wiedmann syndrome: Macrosomia with in utero and postnatal somatic overgrowth, macroglosia, hemihypertrophy, and abdominal wall defect. Hypoglycemia due to hyperinsulinemia. ↑ incidence of tumors.

> **EXAM TIP**
>
> **Beckwith-Weidemann syndrome:** Large babies due to overproduction of IGF-2.

Sexual Development

- Pubertal events are classified by Tanner staging. Puberty progresses usually with an average duration of 3–4 years, spending roughly about 1 year in each stage.
- See Table 16-4 and Figure 16-1.

TABLE 16-4. Tanner Stages

STAGE	BREAST DEVELOPMENT (FEMALE)	GENITAL DEVELOPMENT (MALE)	PUBIC HAIR (FEMALE AND MALE)
I	Preadolescent	Preadolescent	Preadolescent
II	Breast bud (11 years)	Enlargement of scrotum and testes, darkening of scrotum and texture change (12 years)	Sparse, long, slightly pigmented downy hair (female 12, male 13.5)
III	Continued enlargement, no contour separation (12 years)	Enlargement of penis (13 years)	Darker, coarser, and more curled (female 12.5, male 14)
IV	Secondary mound, projection of areola and papilla (13 years)	Increase in penis breadth and development of glans (14 years)	Hair resembles adult, distributed less than adult and not to medial thighs (female 13, male 14.5)
V	Mature stage (15 years)	Mature stage (15 years)	Mature stage (female 14.5, male 15)
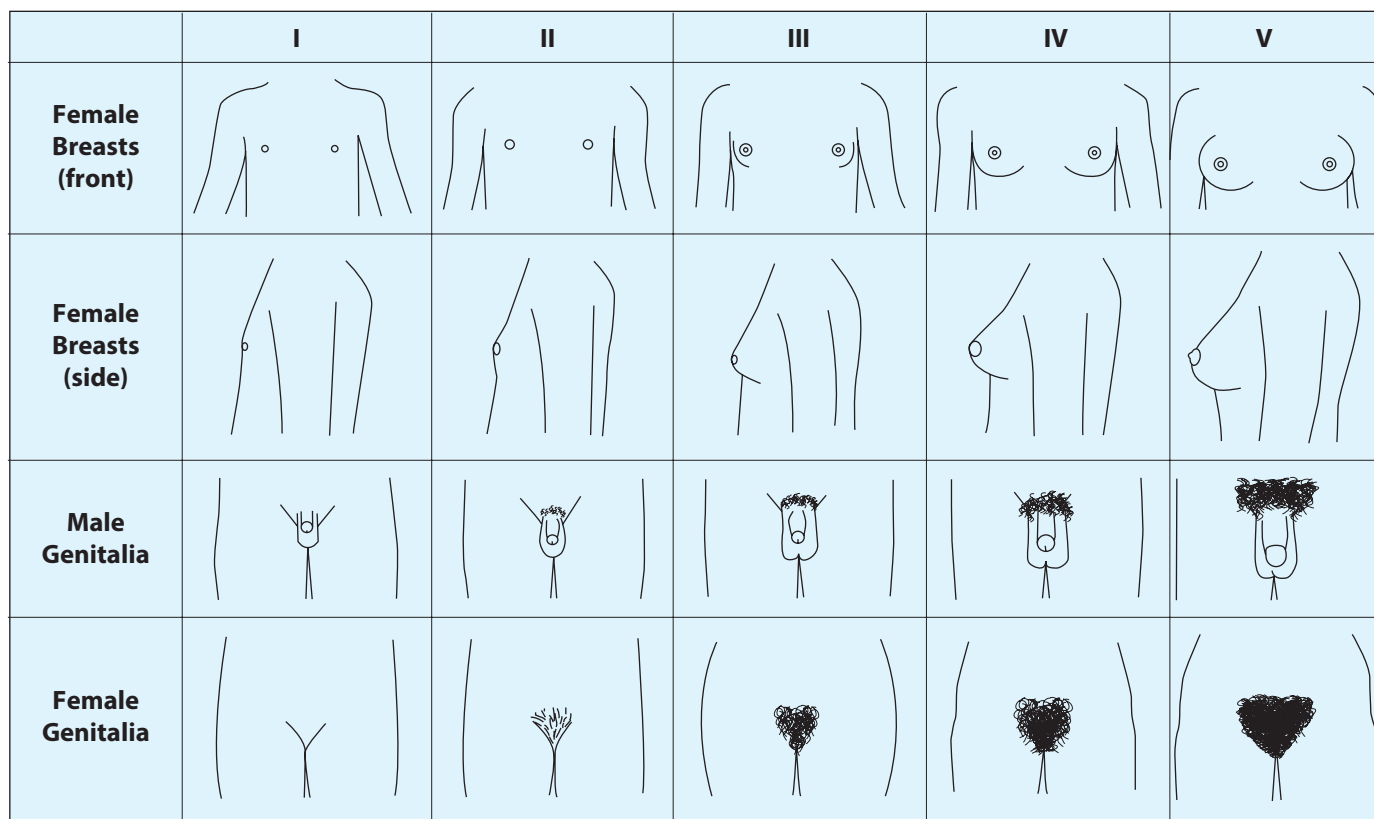
FIGURE 16-1. Tanner stages.

NORMAL FEMALE PROGRESSION

Thelarche → height growth spurt → pubic hair → menarche (12.5–13 years). (In 20 % of girls, pubarche may precede thelarche.)

NORMAL MALE PROGRESSION

Testicular enlargement → pubic hair → penile enlargement → height growth spurt (14–15 years) → axillary hair.

EXAM TIP

The ↑ in height velocity in boys occurs at a later chronologic age than in girls (Tanner IV in boys, Tanner II–III in girls).

A 6½-year-old girl develops enlarged breasts. Six months later she begins to develop pubic and axillary hair. Her menses began at age 9. *Think: Idiopathic precocious puberty.*

Puberty in girls is now recognized to be occurring at earlier age. The exact cause of the precocious puberty in most cases remains unknown. Evaluation should include serum FSH, LH, estradiol, and bone age. Brain MRI should be obtained to rule out possible underlying intracranial cause.

DEFINITION

- Onset of secondary sexual characteristics.
- Girls (<8 years for white girls, <7 for African-American and Hispanics).
- Boys (<9 years).
- Premature breast development (thelarche).
- Premature pubic hair development (pubarche/adrenarche).

ETIOLOGY

Central or True Precocious Puberty
- Premature activation of the hypothalamic-pituitary-gonadal (HPG) axis.
- Gonadotropin dependent: Pubertal (high) FSH and LH and sex steroids (testosterone or estradiol).
- Usually idiopathic in girls, while secondary to organic lesion in boys.
- CNS abnormalities:
  - Hypothalamic hamartoma.
  - Head injury.
  - Hydrocephalus.
  - Radiation.
  - Surgical trauma.
  - Tumors (astrocytoma, glioma, pinealoma, LH-secreting adenoma).

Peripheral or Pseudo Precocious Puberty
- Gonadotropin independent: Prepubertal levels of (low) FSH and LH, pubertal levels of (high) sex steroids (estrogens or androgens).
- HPG axis is not activated.
- Peripheral precocity may be appropriate for child's gender or inappropriate (virilization of females and feminization of males).
- **Male:**
  - Testotoxicosis: Familial male-limited precocious puberty (bilateral testicular enlargement).
  - Tumors:
    - Testicular Leydig cell tumor (unilateral testicular enlargement).
    - Choriocarcinoma, dysgerminoma, hepatoblastoma (human chorionic gonadotropin [HCG] producing).
    - Adrenal tumors (testosterone secreting).
  - CAH.
  - McCune-Albright syndrome.
  - Exogenous sex steroid.
- **Female:**
  - McCune-Albright syndrome: Ovarian cysts secreting estrogen.
  - Tumors:
    - Ovarian tumors (granulosa cell tumor, gonadoblastoma).
    - Choriocarcinoma, dysgerminoma, hepatoblastoma (HCG producing).
  - Adrenal tumors (estrogen secreting).
  - Exogenous sex steroids.

WARD TIP

Most normal 11-year-old girls have pubic hair.

EXAM TIP

Precocious puberty in girls is usually idiopathic, while in boys it usually has an organic cause.

SIGNS AND SYMPTOMS

- Growth acceleration.
- Significantly advanced bone age.
- Sexual development is progressive (in some children, particularly girls, such changes may be very slowly progressive—a variant of normal development).

DIAGNOSIS

- FSH, LH.
- Estradiol, testosterone.
- Dehydroepiandrosterone sulfate (DHEAS), 17-hydroxyprogesterone, androstenedione.
- α-fetoprotein (AFP), HCG.
- Prepubertal levels (low) of gonadotropins and pubertal (high) level of estrogen or testosterone suggest gonadotropin-independent process.
- Gonadotropins may be pubertal or prepubertal at baseline while testosterone or estrogen is usually pubertal in gonadotropin-dependent precocious puberty.
- No ↑ in gonadotropins (LH, FSH) after gonadotropin-releasing hormone (GnRH) agonist stimulation test in gonadotropin-independent precocious puberty.
- Pubertal LH-dominant response (LH > 5 mIU/mL and LH-to-FSH ratio >1) after GnRH agonist stimulation test in true, central, gonadotropin-dependent precocious puberty.
- Pelvic ultrasound to evaluate ovarian and uterine size and rule out any pathology (ovarian cyst, tumor).
- MRI of the head to rule out CNS abnormality in central precocious puberty.
- CT abdomen and pelvis if tumor is the likely cause of peripheral precocious puberty.

TREATMENT

- Treatment of underlying cause (in both central and peripheral puberty).
- GnRH analogues (in central precocious puberty).
- Androgen antagonist (flutamide) and aromatase inhibitor (blocks conversion of androgen to estrogen) in peripheral precocious puberty.

PREMATURE THELARCHE

DEFINITION

- Isolated breast development.
- Most commonly noted during the first 2 years of life.
- May occur after 2 years due to temporary increase in FSH. Breast development is usually limited and often regresses.

SIGNS AND SYMPTOMS

- Normal growth rate and bone age.
- Prepubertal level of gonadotropins and estrogen.

TREATMENT

Nonprogressive and self-limiting.

PREMATURE ADRENARCHE

DEFINITION

Early appearance of sexual hair (premature pubarche) without other signs of sexual development.

- <8 years in girls (<7 years in African-American and Hispanic).
- < 9 years in boys.
- Adult body odor is other associated feature.

ETIOLOGY

- Early onset of increased adrenal androgen production (premature adrenarche).
- In girls it is a risk factor for later development of polycystic ovarian syndrome (PCOS).
- Nonclassical CAH may present similarly and can lead to early puberty.

DIAGNOSIS

- Adrenal androgen (DHEAS): Normal for pubertal stage but elevated for chronologic age.
- If androgens are significantly elevated, CAH and adrenal tumor need to be excluded.

TREATMENT

Self-limiting.

DELAYED PUBERTY

DEFINITION

Absence of pubertal development by 14 years in girls and 15 years in boys.

EPIDEMIOLOGY

More common in boys.

ETIOLOGY

- **Female:**
    - Constitutional.
    - Primary ovarian failure (idiopathic, autoimmune, chemotherapy, radiation, galactosemia, fragile X syndrome, mutation in gonadotropin receptor).
    - Turner syndrome.
    - Hypogonadotropic hypogonadism (Kallmann syndrome).
    - 17-hydroxylase deficiency CAH.
    - Hypopituitarism (congenital or acquired).
    - Dysfunction of HPG axis secondary to systemic illness, undernutrition, or strenuous physical activity.
    - Prader-Willi syndrome.
- **Male:**
    - Constitutional.
    - Primary testicular failure (vanishing testis syndrome, bilateral cryptorchidism/torsion, infection, chemotherapy, radiation, surgical trauma, hemochromatosis, fragile X syndrome, mutation in gonadotropin receptor).
    - Klinefelter syndrome.
    - Hypogonadotropic hypogonadism (Kallmann syndrome).
    - Dysfunction of HPG axis secondary to systemic illness or undernutrition.
    - Hypopituitarism (congenital or acquired).
    - Prader-Willi syndrome.

DIAGNOSIS

- FSH, LH, estradiol, testosterone.
    - Elevated gonadotropin levels (FSH, LH) suggest primary gonadal failure—hypergonadotropic hypogonadism.
    - Low gonadotropin levels suggest hypogonadotropic hypogonadism or constitutional delay. No test definitely differentiates constitutional delay from gonadotropin deficiency until age is well into adolescence.
- Chromosome analysis (for primary gonadal failure).
- MRI of the head (in hypogonadotropic hypogonadism or hypopituitarism).

TREATMENT

- Treatment of the cause.
- Females: Estrogen initially; later, cyclic estrogen–progestin.
- Males: Testosterone.

Menstruation

- The mean age for menarche in an American is 12.8 +/− 1.2 years.
- Menarche occurs about 2–3 years after the initiation of puberty. Two-thirds of females reach menarche at Tanner stage IV puberty.
- Fifty to sixty percent of cycles in the first 2 years after menarche in most girls are anovulatory.
- The length of a cycle is between 21 and 45 days (average is 28 days).
- The length of flow is 2–7 days (average is 3–5 days).
- Blood loss is on average 40 mL (range, 25–70 mL).

AMENORRHEA

Primary Amenorrhea

Lack of spontaneous uterine bleeding regardless of secondary sexual characteristics by age 15 years.

ETIOLOGY

- **Primary ovarian failure** (elevated FSH and LH).
- Chromosomal:
  - Turner syndrome (Gonadal dysgenesis).
  - Triple X syndrome.
  - Pure gonadal dysgenesis (46,XX or 46,XY).
  - Fragile X.
- Classical galactosemia.
- Constitutional delay of puberty.
- Polycystic ovary syndrome.
- Autoimmune oophoritis.
- Radiation.
- Chemotherapy.
- Gonadal trauma.
- 17-hydroxylase deficiency (CAH).
- Congenital lipid hyperplasia.
- FSH/LH receptor mutation.
- Idiopathic.
- **Hypogonadotropic hypogonadism** (low FSH and LH): Isolated or with hypopituitarism.
- Prader-Willi syndrome.
- Anorexia nervosa.
- Strenuous exercise.
- **Structural anomalies:**
  - Imperforate hymen.
  - Agenesis of Müllerian structure (Mayer-Rokitansky-Hauser syndrome).
- Other:
  - Complete androgen insensitivity (testicular feminization syndrome).
  - True hermaphroditism.

Secondary Amenorrhea

Absence of menstruation for 3 months in females with previous history of regular menses or 6 months in females with irregular menses.

> A 16-year-old female had the onset of breast development at the age of 12 years and menses at age 14. She has not had menses for 2 months. She is active in sports. Physical examination is normal. *Think: Rule out pregnancy, then consider the sports contribution to her secondary amenorrhea.*
>
> Pregnancy is the most common cause of amenorrhea and should be excluded in any female patient of reproductive age. After pregnancy, thyroid disease and hyperprolactinemia should be considered as potential diagnoses. Amenorrhea can also occur due to exercise and participation in athletic activity. Female athlete triad (disordered eating, amenorrhea, and osteoporosis) is a well-recognized entity. Athletic amenorrhea is due to hypothalamic-pituitary axis suppression, but it is a diagnosis of exclusion. Other causes must be excluded, and evaluation should include pregnancy test, prolactin, FSH, LH, TSH, T_4, DHEAs, 17 hydroxyprogesterone, and testosterone levels.

ETIOLOGY

- Pregnancy.
- Turner syndrome (mosaicism).
- Hyperandrogenic states (PCOS, CAH).
- Hyperprolactinemia.
- Hypothalamic amenorrhea.
- Causes of primary amenorrhea.

DIFFERENTIAL DIAGNOSIS

- **Normal/low FSH:**
  - Consider hypothalamic amenorrhea related to stress, weight loss, an eating disorder, competitive athletics, phenothiazine use, or substance abuse.
  - Also consider chronic disease, CNS tumor (i.e., prolactinoma), pituitary infiltration or infarction as in postpartum hemorrhage or sickle cell disease, and Asherman syndrome (following endometrial curettage).
- **High FSH:** Consider gonadal dysgenesis as in mosaic Turner syndrome, autoimmune oophoritis, or primary ovarian insufficiency.

DYSMENORRHEA

DEFINITION

Recurrent, crampy lower abdominal pain during menstruation.

Primary or Essential Dysmenorrhea

Dysmenorrhea, in the absence of any specific, pelvic pathologic condition. Associated with ovulatory cycles.

ETIOLOGY

- Progesterone produced during ovulatory cycle ↑ the synthesis of the prostaglandins.
- Excessive amounts of prostaglandins F_2 and E_2, which cause uterine contractions, tissue hypoxia and ischemia, and ↑ sensitization of pain receptors.

WARD TIP

The most common causes of secondary amenorrhea include pregnancy, stress, and PCOS.

WARD TIP

Dysmenorrhea is the most common gynecologic complaint.

*T*REATMENT

Based on severity of symptoms and degree of daily life restrictions, recommend prostaglandin inhibitors (NSAIDs) for dysmenorrhea at the onset of flow or pain and/or estrogen–progestin oral contraceptives or if severe, a combination of both.

Secondary Dysmenorrhea

*E*TIOLOGY

- Underlying structural abnormality of the vagina, cervix, or uterus (endometrial polyps, fibroids).
- Congenital anomalies.
- Pelvic adhesions.
- Endometriosis.
- Foreign body such as an intrauterine device.
- Endometritis: Infection, especially secondary to sexually transmitted diseases (STDs).
- Complications of pregnancy such as ectopic pregnancy.

Testicular Feminization

*D*EFINITION

- Androgen insensitivity syndrome (complete and partial form).
- X-linked recessive inheritance.
- In complete androgen insensitivity syndrome, XY male appears as unambiguous female with a short, blind-ending vaginal pouch and no uterus, female phenotype but 46 XY karyotype with normal breast development, and testosterone concentrations in the normal adult male range. Androgen receptor (AR) is either absent or unable to bind androgen.
- In partial androgen insensitivity syndrome, XY cases have either ambiguous or female genitalia with no uterus. Considerable virilization occurs at puberty, but gynecomastia also develops. Androgen receptor binding is low or normal.

*S*IGNS AND *S*YMPTOMS

- Primary amenorrhea.
- Normal breast development.
- Pubic hair absent or sparse.
- Presence of testes in inguinal canal or abdomen.

*D*IAGNOSIS

- Testosterone level is elevated.
- LH is normal or elevated.
- Sex hormone binding globulin (SHBG) test: IM testosterone (2 mg/kg) unable to suppress SHBG to <80% of the basal value suggests androgen insensitivity.
- HCG stimulation (3000 mg/m^2/day) every other day for 2 days shows normal testosterone response (double from baseline at 48 hours, then double again 2 days after the second injection) and helps differentiate partial androgen sensitivity from causes of ambiguous genitalia due to testosterone synthesis defect.
- Androgen receptor binding studies in cultured genital skin fibroblast.
- DNA analysis for mutation in AR gene.

True Hermaphroditism

DEFINITION

- Now known as ovotesticular disorder of sex development (DSD).
- Gonads comprised of both ovarian and testicular elements (ovotestis).
- Most are 46,XX.
- Can be familial.

ETIOLOGY

Abnormal gonadal differentiation.

SIGNS AND SYMPTOMS

- Ambiguous genitalia—significant masculinization (raised as male).
- Risk of malignant transformation of gonadal tissue is much lower (2%) than XY gonadal dysgenesis.

Pseudohermaphroditism

FEMALE

DEFINITION

Normal gonads and uterus (both gonads are ovaries) with virilization of external genitalia in a patient with a 46,XX karyotype.

ETIOLOGY

- CAH (21-hydroxylase deficiency, 11 β-hydroxylase deficiency, 3 β-hydroxysteroid dehydrogenase deficiency).
- Placental aromatase deficiency (conversion of androgens to estrogens is blocked). Estriol level is undetectable. Maternal virilization during pregnancy.
- Luteoma of pregnancy: Maternal virilization during pregnancy.

SIGNS AND SYMPTOMS

Virilization of external genitalia (clitoral hypertrophy, labioscrotal fusion).

MALE

DEFINITION

Normal testes (both gonads are testes) with undervirilization or completely female appearing external genitalia in a patient with 46,XY karyotype.

ETIOLOGY

- Androgen insensitivity.
- CAH: 3β-hydroxysteroid dehydrogenase deficiency, 17-hydroxylase deficiency, and congenital lipoid adrenal hyperplasia.
- Enzyme defects in testosterone synthesis (17-ketoreductase deficiency).
- 5α-reductase deficiency: Conversion of testosterone to dihydrotestosterone is blocked.

SIGNS AND SYMPTOMS

Undervirilization of external genitalia (small phallus, hypospadias, undescended testes) or completely female appearing genitalia.

Gender Identity Disorder

- Some children have a gender identity that does not correlate with their assigned genotypic gender (see Psychiatric Disease chapter for more information). While there are different views on whether gender nonconformity is a normal variation of gender expression, a medical disease, or a psychiatric disease, it is even more unclear as to how these children should be treated.
- As these children enter into puberty and adolescence, there may be a desire for medical interventions to change their gender presentation. Increasingly, pediatric endocrinologists are being asked to hormonally suppress or induce phenotypic appearances to correlate with their chosen gender identity.
- Treatment
    - Close collaboration with mental health providers is essential.
    - Suppression of puberty: Initiated ideally in Tanner stage 2 to suppress the onset or progression of puberty with the use of GnRH essentially preventing the development of unwanted sexual features. Also allows time for child to determine if he or she wants to initiate gender affirming hormonal therapy.
    - Gender affirming hormonal therapy: Initiated usually by age 16 to induce pubertal development to the identified gender the child has chosen allowing for the desired phenotypic appearance.

Neurologic Disease

Seizures

DEFINITION

- A paroxysmal electrical discharge of neurons in the brain resulting in an alteration of function or behavior.
- The most common neurologic disorder in children:
    - 4–10% of children.
    - 1% of all ED visits.
- Highest incidence: <3 years.

ETIOLOGY

Multiple etiologies have been identified for seizures. Provoked causes include:
- Fever.
- Metabolic:
    - Hypoglycemia.
    - Hyponatremia.
    - Hypocalcemia.
    - Inborn errors of metabolism.
- Medications and illegal drugs.
- Trauma (intracranial hemorrhage).
- Infections (encephalitis, meningitis, abscess).
- Vascular events (strokes).
- Hypoxic ischemia encephalopathy.
- Idiopathic.

TYPES OF SEIZURES

See Table 17-1.

Partial (Focal) Seizures

Begin in one brain region.
1. Simple partial seizures:
    - Average duration is 10–20 seconds.
    - Restricted at onset to one focal cortical region.
    - Consciousness is not altered.
    - Tend to involve the face, neck, and extremities.
    - Patients may complain of aura, which is characteristic for the brain region involved in the seizure (i.e., visual aura, auditory aura, etc.).
    - Seizures can also be somatosensory/visual or auditory.

TABLE 17-1. **Types of Seizures**

Absence	Sudden brief discontinuation of activity and unresponsiveness
Tonic-Clonic	Bilateral symmetrical tonic contraction, then bilateral clonic contractions
Tonic	Sustained muscle contraction for seconds to minutes
Clonic	Repetitive, rhythmic myoclonus at 2–3 Hz
Myoclonic	Sudden, brief (< 100 ms) involuntary contraction of muscles or group of muscles
Atonic	Sudden, brief, 1–2 sec ↓ in tone without preceding myoclonic or tonic event

---

WARD TIP

The diagnosis of clinical epilepsy requires two or more unprovoked seizures.

EXAM TIP

- Recurrence risk after a first unprovoked episode is 45% (27–52%).
- The risk of epilepsy is >70% after two unprovoked episodes.

EXAM TIP

In most children with seizures, an underlying cause cannot be determined and a diagnosis of idiopathic epilepsy is given.

EXAM TIP

Partial seizures: Onset in one brain region. Generalized seizures: Onset simultaneously in both cerebral hemispheres.

EXAM TIP

Aura: Abnormal perception or hallucination, which occurs before consciousness is lost and for which memory is returned afterwards. In seizure, as opposed to migraine, the aura is part of the seizure.

2. Complex partial seizures:
   - Average duration is 1–2 minutes.
   - Hallmark feature is *alteration* or loss of consciousness.
   - Automatisms are seen in 50–75% of cases (psychic, sensory, or motor phenomena).
3. Secondarily generalized seizures:
   - Starts as a partial seizure in a focal area of the brain and then spread to the entire brain leading to a generalized seizure.
   - Sometimes the person does not recall the first part of the seizure.
   - Occurs in >30% of people with partial epilepsy.

Generalized Seizures

Begins simultaneously in both cerebral hemispheres. Consciousness is impaired from seizure onset.

1. Typical absence seizures (formerly "petit mal"):
   - Generalized seizure.
   - Characterized by sudden cessation of motor activity or speech.
   - Brief stares (usually <10 seconds), rarely longer than 30 seconds.
   - More common in girls. Male-to-female ratio: 2:1.
   - Onset 4-10 years.
   - Can occur many times throughout the day.
   - There is no aura.
   - There is no postictal state.
   - Seizure can be elicited by hyperventilation.
   - Childhood absence epilepsy is associated with characteristic 3-Hz spike-and-wave pattern (Figure 17-1) on EEG.
2. Generalized tonic-clonic (GTC, formerly "grand mal") seizures:
   - Extremely common and may follow a partial seizure with focal onset.
   - Patients suddenly lose consciousness, their eyes roll back, and their entire musculature undergoes tonic contractions, rarely arresting breathing.
   - Gradually, the hyperextension gives way to a series of rapid clonic jerks.
   - Finally, a period of flaccid relaxation occurs, during which sphincter control is often lost (incontinence).
   - Prodromal symptoms (not aura) often precede the attack by several hours and include mood change, apprehension, insomnia, or loss of appetite. (Unclear if these are warning signs or part of the cause.)

> **EXAM TIP**
>
> Both simple and complex partial seizures may become generalized.

> **WARD TIP**
>
> The first step in evaluating any seizure disorder is determining the type of seizure.

> **EXAM TIP**
>
> Motor activity is the most common symptom of simple partial seizures.

> **EXAM TIP**
>
> The presence of an aura always indicates a focal onset of the seizure. Physiologically, an aura is simply the earliest conscious manifestation of a seizure and corresponds with area of brain involved.

FIGURE 17-1. **Absence seizure EEG.** Characteristic 3-Hz spike and wave pattern.

Absence Versus Complex Partial Seizures

While examining an 8-year-old girl in your office, the child suddenly develops a blank stare and flickering eyelids. Twenty seconds later she returns to normal and acts as if nothing out of the ordinary has occurred. *Think: Absence seizure.*

You are reviewing the history before seeing a patient. She is a 7-year-old bright girl with no significant past medical history. The schoolteacher noted that she sometimes does not respond when her name is called. Also, she stares in space with a blank look momentarily. *Think: Absence seizures.*

PEDIATRIC SEIZURE DISORDERS

Simple Febrile Seizure

- The most common seizure disorder during childhood.
- Occurs in approximately 2–4% of children younger than 5 years with a peak incidence between 12 and 18 months.
- Present as a brief tonic-clonic seizure associated with a fever.
- Risk of recurrence is 30% after first episode and 50% after second episode.
- Highest recurrence if episode before 1 year of age (50%).
- Antipyretics do not appear to prevent the onset of future febrile seizures.
- There are no long-term sequelae, and most children will outgrow by age 6.
- Risk of epilepsy (1–2% as opposed to 0.5–1% in the general population) not statistically significant.
- ↑ risk of epilepsy (up to 13%) in the presence of:
  - Abnormal neurologic examination.
  - Complex febrile seizure (lasting >15 minutes, focal in nature, and/or recurrent seizure within 24 hours).
  - Family history of epilepsy.
- Among first-degree relatives 10–20% of parents and siblings also have had febrile seizures. An autosomal-dominant inheritance pattern with incomplete penetrance is demonstrated in some families (19p and 8q13–21).
- Consider meningitis or toxin exposures for a febrile seizure >15 minutes. Have a greater consideration for spinal tap in infants <1 year of age or in those with clinical signs of meningitis.

Neonatal Seizure

- The most common neurologic manifestation of impaired brain function.
- **Occurs in 1.8–3.5** of every 1000 newborns.
- Higher incidence in low-birth-weight infants.
- Metabolic, toxic, hypoxic, ischemic, and infectious diseases are commonly present during the neonatal period, placing the child at an ↑ risk for seizures.
- Myelination is not complete at birth; thus, GTC seizures are very uncommon in the first month of life.
- May manifest as tonic, myoclonic, clonic, or subtle (prolonged nonnutritive sucking, nystagmus, color change, autonomic instability).
- EEG may show burst suppression (alternating high and very low voltages), low-voltage invariance, diffuse or focal background slowing, and focal or multifocal spikes.
- Neonatal seizures are typically treated acutely with phenobarbital (drug of choice), fosphenytoin, or benzodiazepines.
- Phenytoin not a first-line agent due to depressive effect on the myocardium and variable metabolism in newborns.

- Other antiseizure drugs, such as levetiracetam or topiramate, are being increasingly used for treatment of neonatal seizures but are not yet considered evidence-based first-line agents.

Infantile Spasm

- Onset: 4–7 months.
- Clusters of brief rapid symmetric flexor/extensor contractions of the neck, trunk, and extremities up to 100 per day. Clusters can last <1 minute to 10–15 minutes.
- Symptomatic type is most commonly seen with central nervous system (CNS) malformations, brain injury, tuberous sclerosis, or inborn errors of metabolism, and typically has a poor outcome.
- Cryptogenic type has a better prognosis and children typically have an uneventful birth history and reach developmental milestones before the onset of the seizures.
- Treated with adrenocorticotropic hormone (ACTH) in the United States.
- Vigabatrin (equally as effective as ACTH therapy).
- EEG has characteristic hypsarrhythmia pattern: Large-amplitude chaotic multifocal spikes and slowing (see Figure 17-2).

EPILEPSY

DEFINITION

- A history of two or more unprovoked seizures.
- After a nebulous period (on the order of 5–10 years) of seizure freedom without the aid of antiepileptic medications or devices, the epilepsy can be considered to have resolved, particularly if the patient fits an epilepsy syndrome that is known typically to resolve.
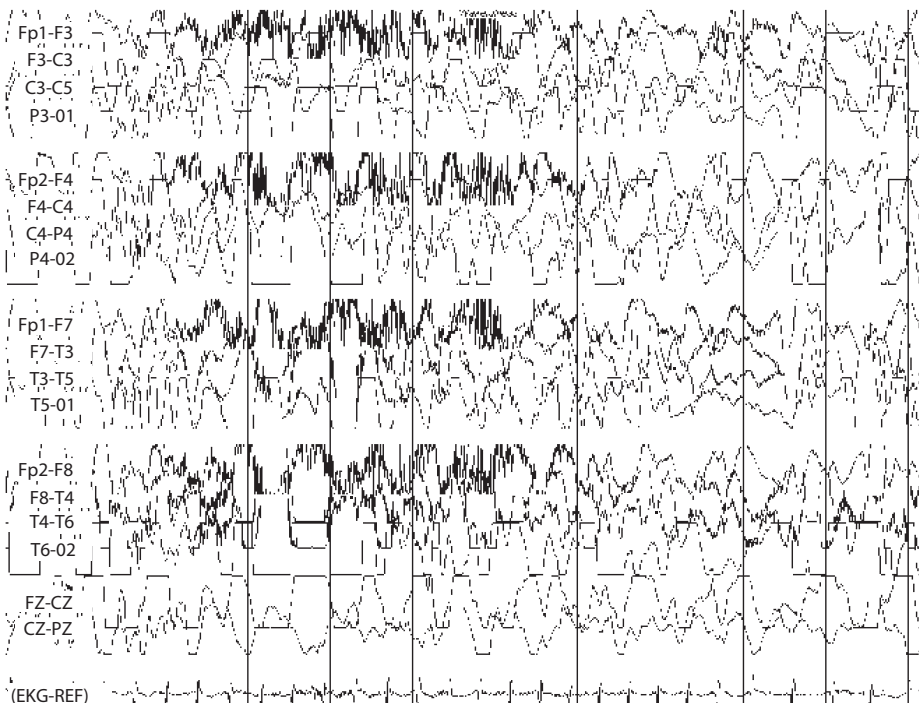
FIGURE 17-2. EEG demonstrating hypsarrhythmia pattern. Often seen in tuberous sclerosis, for example.

EPIDEMIOLOGY

Epilepsy occurs in 0.5–1% of the population and begins in childhood in 60% of the cases.

SIGNS AND SYMPTOMS

- Vary depending on the seizure pattern. See above discussion of types of seizures.
- A seizure is defined electrographically as a hypersynchronous, hyperrhythmic, high-amplitude signal that evolves in both frequency and space.
- An aura is a stereotyped symptom set that immediately precedes the onset of a clinical seizure and does not affect consciousness.
- Physiologically, the aura is the true beginning of the seizure, and as such its character can be quite useful for localizing seizure onset.
- A seizure prodrome is a set of symptoms, much less stereotyped than an aura, that precedes a seizure by hours to days. Symptoms such as headache, mood changes, and nausea are reported by over 50% of patients in some series.

TREATMENT

- Therapy is directed at preventing the attacks.
- See Table 17-2 for current pharmacologic treatments for epilepsy.

COMMON EPILEPSY SYNDROMES

See Table 17-3 for localizing/lateralizing seizure semiologies.

Localization-Related Epilepsy

- Seizures secondary to a focal CNS lesion, not necessarily visible on imaging, best candidates for epilepsy surgery.
- Common examples include masses (particularly cortical tubers of tuberous sclerosis [TS]), cortical dysplasia, postencephalitic gliosis, and arteriovenous malformations (AVMs).

TABLE 17-2. Epilepsy Drugs and Their Use in Different Seizure Types

DRUG (U.S. BRAND NAME)	SEIZURE TYPE	SIDE EFFECTS
Carbamazepine (Tegretol, Carbatrol)	Focal-onset	Aplastic anemia
Ethosuxamide (Zarontin)	Absence, some generalized	Drowsiness
Phenytoin (Dilantin)	Generalized or focal	Stevens-Johnson, gingival hyperplasia
Phenobarbital	Focal, generalized	Hyperactivity
Valproate (Depakote, Depacon)	Generalized, focal-onset	Hepatic failure, low platelets, pancreatitis
Topiramate (Topamax)	Partial, generalized	Renal stones, weight loss
Levetiracetam (Keppra)	Partial, generalized, Lennox-Gastaut	Behavior change
Lamotrigine (Lamictal)	Focal, generalized	Stevens-Johnson syndrome
Zonisamide (Zonigran)	Focal, generalized	Don't use if sulfa allergic
Felbamate (Felbatol)	Focal, generalized	Hepatic failure, aplastic anemia

TABLE 17-3.   Localizing/Lateralizing Seizure Semiologies

Clinical Event	Lateralization	Localization
Ipsilateral indicates phenomenon is directed toward the seizing hemisphere.		
Head turn		
Early nonforced	Ipsilateral	Temporal
Forced		
Early forced		Frontal (less likely to generalize)
Late forced	Contralateral	Temporal (more likely to generalize)
Ocular version	Contralateral	Occipital
Focal clonus	Contralateral	Frontal = temporal
Dystonic limb	Contralateral	Temporal > frontal
Unilateral tonic limb	Contralateral	
M2e fencing	Contralateral	Frontal > temporal
Figure 4	Contralateral	
Ictal paresis	Contralateral	
Todd's (postictal) paresis	Contralateral	
Unilateral blinking	Ipsilateral	
Unilateral automatism	Ipsilateral	
Postictal nose rubbing	Ipsilateral (to hand used)	Temporal > frontal
Postictal cough		Temporal
Bipedal automatism		Frontal > temporal
Hypermotoric state		Supplementary motor area
Ictal spitting	Right	Temporal
Automatism with preserved responsiveness	Right	Temporal
Gelastic		Hypothalamic, mesial temporal
Ictal vomiting/retching	Right	Temporal
Ictal urinary urgency	Nondominant	Temporal
Loud vocalization		Frontal > temporal
Ictal speech arrest		Temporal
Postictal aphasia	Dominant	

Benign Epilepsy with Centrotemporal spikes (BECTS)

> A 5-year-old boy was noted to have facial twitching and facial drooling at a day care center during a nap followed by generalized shaking of the body lasting 1–2 minutes. The mother also reported noticing facial twitching during sleep. In the ED, he is awake and his neurological examination is normal. You order an EEG, which shows centrotemporal spikes. *Think: BECTS formerly known as benign rolandic epilepsy.*
>
> BECTS is a partial epilepsy of childhood. The usual age of presentation is 3–13 years. Typical presentation: Seizure occurs during sleep (nighttime) with facial involvement. EEG shows central temporal spikes. Seizures typically resolve spontaneously by early adulthood.

- Most common partial epilepsy.
- Onset 3–13 years.
- Particularly nocturnal (early morning hours before awakening).
- EEG: Central temporal spikes (Figure 17-3).
- Excellent prognosis; most resolve by age 16 years.
- **Treatment:** Carbamazepine, phenytoin, and valproic acid.

West Syndrome

- Two percent of childhood epilepsies, but 25% of epilepsy with onset in the first year of life.
- Onset is at age 4–8 months.
- Triad: Infantile spasms, mental retardation (MR), and hypsarrhythmia.
- Boys are more commonly affected but not significantly; generally poor prognosis.
- Differential includes TS (largest group), CNS malformation, intrauterine infection, inborn metabolic disorders, and idiopathic. Idiopathic group fares the best.
- **Treatment** in the United States is restricted to ACTH.

Juvenile Myoclonic Epilepsy (JME)

- Onset: 12–16 years.
- Characteristic history: Usually early morning on awakening, while hair combing and tooth brushing.

FIGURE 17-3. EEG demonstrating central temporal spikes characteristic of benign Rolandic epilepsy.
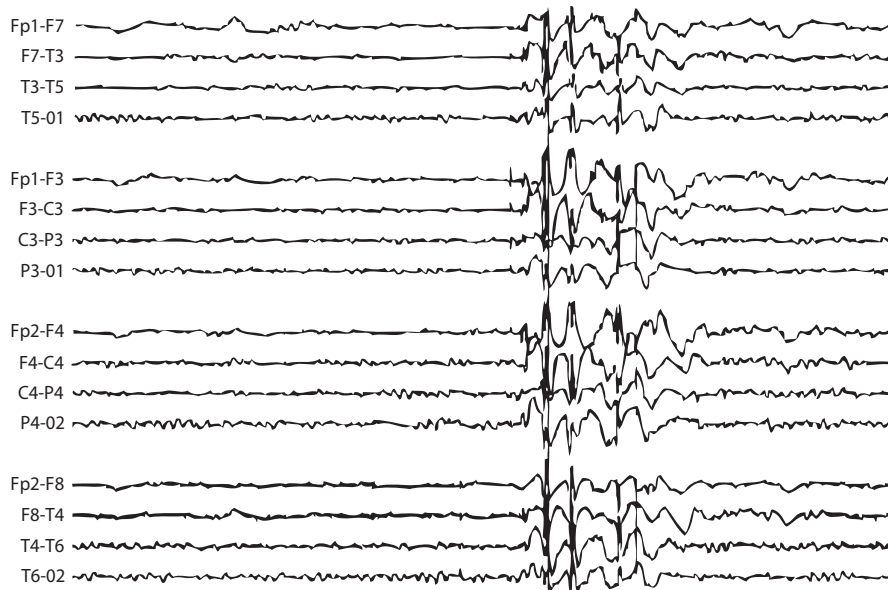
FIGURE 17-4. **EEG demonstrating characteristic pattern of juvenile myoclonic epilepsy.**

- Seizures: Myoclonus, absence, GTC.
- EEG: 4- to 6-Hz irregular spike-and-wave pattern (Figure 17-4 and Table 17-4).
- Treatment: Valproate, lamotrigine.
- Prognosis: Good Rx response but lifelong.
- High rate of recurrence if antiepileptic drug (AED) discontinued.

Childhood Absence Epilepsy (CAE; Pyknolepsy)

- See absence seizures above. GTC seizures often develop in adolescence; spontaneous resolution is the rule, however.
- Juvenile absence epilepsy (JAE): Similar to CAE except beginning in adolescence and have more GTC seizures, sexes affected equally, EEG spike and wave often faster than 3 Hz.

Lennox-Gastaut Syndrome (LGS)

- A generalized epilepsy syndrome.
- Multiple seizure types (tonic, atonic, absence, and myoclonic seizures).
- EEG: 1.5- to 2.5-Hz spike-and-wave pattern.
- Cognitive impairment.
- Infantile spasms may evolve to LGS (30%).
- Seizures are frequent and resistant to treatment with AEDs.

Landau-Kleffner Syndrome (LKS; Acquired Epileptic Aphasia)

- Language regression.
- Aphasia (primarily receptive or expressive).
- Seizures of several types (focal or GTC, atypical absence, partial complex).
- EEG: High-amplitude spike-and-wave discharges. Obtain EEG during sleep (more apparent during non-rapid eye movement sleep).
- **Differential diagnosis:** Autism.
- **Treatment:** Valproic acid.

Progressive Myoclonic Epilepsies

- This group of diseases includes Unverricht-Lundborg disease, myoclonic epilepsy with ragged-red fibers (MERRF), Lafora disease, neuronal ceroid lipofuscinosis, and sialidosis/mucolipidosis, and Ramsay Hunt syndrome.

WARD TIP

Loss of language skills in a previously normal child with seizure disorder. *Think: LKS.*

WARD TIP

Evaluate patients following their first seizure (for mass, lesion, etc.) prior to diagnosing and treating epilepsy.

TABLE 17-4. **Characteristic EEG Patterns in Various Seizure Conditions**

SEIZURE CONDITION	EEG	DRUG OF CHOICE
Simple febrile seizure Brief GTC with complete rapid recovery	Not required	Reassurance
Complex partial seizure > 15 min, focal, recurrent	Not required *Get MRI if focal prolonged*	Rectal valium (Diastat®) if recurrent
Infantile spasms (IS) See above	Hypsarrythmia	ACTH
West syndrome Hypsarrythmia, IS, mental retardation	Hypsarrythmia	ACTH
Benign myoclonus of epilepsy Clinically similar to IS but resolves in 3 months, rare after 2 yr	Normal	—
Benign myoclonic epilepsy 4 months–2 yr, brief myoclonic activity or neck and legs flexion with arms extension	3-Hz spike/polyspike and wave	Valproate Levetiracetam is safer in young
Benign rolandic epilepsy See above	Central-temporal spikes	—
Juvenile myoclonic epilepsy See above	4- to 6-Hz generalized polyspike/wave with photo-paroxysmal response	Valproate Lamotrigine
Childhood absence epilepsy See above	3-Hz spike and wave (first second may be 4 Hz, then ↓ to 2.5 by end)	Ethosuximide Carbamazepine contraindicated
Juvenile absence epilepsy See above	3- to 3.5-Hz spike and wave	Valproate
Lennox-Gastaut syndrome See above	1.5- to 2.5-Hz spike and wave	Valproate Clonazepam Vigabatrin
Landau-Kleffner syndrome See above	Generalized spike and wave, 1.5- to 3-Hz range	Benzodiazepines Valproate
Mesial temporal sclerosis See above	5–7 Hz, rhythmic, sharp theta activity	Phenytoin, phenobarbital, carbamazepine, and valproate

- Begin in late childhood to adolescence, and entail progressive neurologic deterioration with myoclonic seizures, dementia, and ataxia. Death within 10 years of onset is common, but survival to old age occurs.

Mesial Temporal Sclerosis/Temporal Lobe Epilepsy

- Gliotic scarring and atrophy of the hippocampal formation, creating a seizure focus. Abnormality is often apparent on high-resolution magnetic resonance imaging (MRI).

- Rhythmic, 5–7 Hz, sharp theta activity.
- Phenytoin, phenobarbital, carbamazepine, and valproate are equally effective. Curative resection is often possible if refractory to treatment.

Rett Syndrome

DEFINITION

A neurodegenerative disorder of unknown cause.

EPIDEMIOLOGY

- X-linked recessive with *MECP2* gene mutation occurs almost exclusively in females. Rett syndrome does exist in males with 47,XXY and *MEP2* gene mutation. However, males with 46,XY and *MECP2* gene mutation do not survive.
- Prevalence: 1 in 15,000 to 1 in 22,000.

ETIOLOGY

- Most cases result from defect in *MECP2*. Gene testing is available.
- *CDKL5* gene mutations can also cause Rett syndrome.

SIGNS AND SYMPTOMS

- Normal development until 12–18 months (can appear as early as 5 months).
- The first signs are deceleration of head growth, lack of interest in environment, and hypotonia, followed by a regression of language and motor milestones.
- Ataxia, hand-wringing, reduced brain weight, and episodes of hyperventilation are typical.
- Autistic behavior.

PROGNOSIS

- After the initial period of regression, the disease appears to plateau.
- Death occurs during adolescence or the third decade of life (cardiac arrhythmias).

> **EXAM TIP**
>
> The hallmark of Rett syndrome is repetitive hand-wringing and loss of purposeful and spontaneous hand movements.

Status Epilepticus (SE)

DEFINITION

Any seizure or recurrent seizures without return to baseline lasting >20 minutes.

ETIOLOGY

- Febrile seizures, idiopathic status epilepticus, and symptomatic SE.
- Febrile SE accounts for 5% of febrile seizures and one-third of all episodes of SE.

PATHOPHYSIOLOGY

Prolonged neural firing may result in neuronal cell death, called excitotoxicity.

TREATMENT

- Initial treatment includes assessment of the respiratory and cardiovascular systems (ABCs).
- Obtain rapid bedside glucose level.

> **EXAM TIP**
>
> In children under age 3, febrile seizures are the most likely etiology of status epilepticus.

MANAGEMENT

- **Stabilization phase** (0–5 minutes of seizure activity): Airway, breathing, circulation (ABCs); give O_2; obtain IV acess, monitor vital signs, obtain rapid bedside glucose; obtain additional labs and cultures as indicated.
- **Initial therapy phase** (5–20 minutes of seizure activity): Administer a benzodiazepine (specifically IM midazolam, lorazepam, or diazepam, OR Intranasal [IN] midazolam or buccal midazolam if IV access not obtained). Benzodiazepines are recommended as the initial therapy of choice, given its demonstrated efficacy, safety, and tolerability.
- **Second therapy phase** (20–40 minutes of seizure activity): If seizure continues, other options include fosphenytoin, valproic acid, and levetiracetam. IV phenobarbital is an alternative if none of the three recommended therapies are available, but can worsen respiratory depression.
- **Third therapy phase** (40+ minutes of seizure activity): If seizure continues, treatment considerations should include repeating second-line therapy or anesthetic doses of either thiopental, midazolam, pentobarbital, or propofol (all with continuous EEG monitoring).

Neuro-Cutaneous Syndromes

STURGE-WEBER SYNDROME

Dermato-oculo-neural syndrome.

EPIDEMIOLOGY

Occurs sporadically in 1 in 50,000.

ETIOLOGY

- Abnormal development of the meningeal vasculature, resulting in hemispheric vascular steal phenomenon and resultant hemiatrophy.
- Facial capillary hemangioma usually accompanies in V1 distribution.

SIGNS AND SYMPTOMS

- Cutaneous facial nevus flammeus (distribution of the trigeminal nerve) → port-wine stain.
- Ipsilateral diffuse cavernous hemangioma of the choroid → glaucoma.
- Ipsilateral meningeal hemangiomatosis (seizures and mental retardation).
- The lesions in the eye, skin, and brain are always present at birth.
- Contrast-enhanced MRI to look for meningeal angioma.
- Seizures are usually refractory, and hemispherectomy improves the prognosis.
- It is very unlikely to have meningeal involvement without port-wine stain, but most children with a facial port-wine nevus do not have an intracranial angioma.

VON HIPPEL–LINDAU DISEASE

DEFINITION

A neurocutaneous syndrome (usually no cutaneous involment) affecting many organs, including the cerebellum, spinal cord, medulla, retina, kidneys, pancreas, and epididymis.

SIGNS AND SYMPTOMS

The major neurologic manifestations are:
- **Cerebellar/spinal hemagioblastomas:** Present in early adult life with signs of ↑ ICP.

- **Retinal angiomata:** Small masses of thin-walled capillaries in the peripheral retina.
- Multiple congenital cysts of the pancreas and polycythemia are also associated with it.
- Early detection and resection is the best management.
- Photocoagulation for retinal detachment.

NEUROFIBROMATOSIS (NF)

EPIDEMIOLOGY

Both types display autosomal-recessive inheritance patterns.
- **Type 1:** The most prevalent type (~90%) with an incidence of 1 in 4000 (chromosome 17).
- **Type 2:** Accounts for 10% of all cases of NF, with an incidence of 1 in 40,000 (chromosome 22).

CLINICAL MANIFESTATIONS

Type 1
- Diagnosis is made by the presence of two or more of the following:
    - Six or more café-au-lait macules (must be >5 mm prepuberty, >15 mm postpuberty).
    - Axillary or inguinal freckling (Crowe sign).
    - Two or more iris Lisch nodules (melanocytic hamartomas).
    - Two or more cutaneous neurofibromas.
    - A characteristic osseous lesion (sphenoid dysplasia, thinning of long-bone cortex).
    - Optic glioma.
    - A first-degree relative with confirmed NF-1.
- Learning disabilities, abnormal speech development, and seizures are common.
- Patients are at a higher risk for other tumors of the CNS such as meningiomas and astrocytomas (optic nerve gliomas in 20%) (but not as significantly as in NF-2).
- Risk of malignant transformation to neurofibrosarcoma is <5%.

Type 2
- Diagnosis is made when one of the following is present:
    - Bilateral CN VIII masses (most of the cases).
    - A parent or sibling with the disease and either a neurofibroma, meningioma, glioma, or schwannoma.
- Café-au-lait spots and skin neurofibromas are not common findings.
- Patients are at significantly higher risk for CNS tumors than in NF-1 and typically have multiple tumors.

TREATMENT

Treatment is mainly aimed at preventing future complications and early detection of malignancies. Resection of the schwannomas can be done to preserve hearing.

TUBEROUS SCLEROSIS

EPIDEMIOLOGY

- Inherited as an autosomal-dominant trait, with a frequency of 1:6,000.
- Two-thirds are new mutations.

> **EXAM TIP**
>
> About 50% of NF-1 results from new mutations. Parents should be carefully screened before counseling on the risk to future children.

> **WARD TIP**
>
> NF-1: Café-au-lait spots, childhood onset. NF-2: Bilateral acoustic neuromas, teenage onset, multiple CNS tumors.

> **EXAM TIP**
>
> Café-au-lait is French for "coffee with milk," which is the color of these lesions.

> **EXAM TIP**
>
> Prenatal diagnosis and genetic confirmation of diagnosis are available in familial cases of both NF-1 and NF-2, but not new mutations.

PATHOLOGY

- Characteristic brain lesions consist of tubers, which are located in the convolutions of the cerebrum, where they undergo calcification and project into the ventricles.
- There are two recognized genes: TSC1 on chromosome 9, encoding a protein called hamartin; and TSC2 on chromosome 16, encoding a protein called tuberin.
- Tubers may obstruct the foramen of Monro, → hydrocephalus.

CLINICAL MANIFESTATIONS

- Hypopigmented macules (Ash leaf skin lesions) are seen in 90% and are best viewed under a Wood's lamp (violet/ultraviolet light source).
- CT scan shows calcified hamartomas (tubers) in the periventricular region.
- Seizures and infantile spasms (IS) are common. Seizures usually present as IS before age 1 and are difficult to control. Children develop autistic features and have developmental disabilities and learning difficulties.
- Adenoma sebaceum—small, raised papules resembling acne that develop on the face in butterfly pattern between 4 and 6 years of age, actually are small hamartomas.
- A Shagreen patch (rough, raised, leathery lesion with an orange-peel consistency in the lumbar region) is also a classic finding; typically does not develop until adolescence.
- Fifty percent of children also have rhabdomyomas of the heart, which may → CHF or arrhythmias. They can be found on prenatal ultrasonography but usually regress after birth.
- Hamartomas of the kidneys and the lungs are also frequently present.

DIAGNOSIS

- A high index of suspicion is needed, but all children presenting with infantile spasms should be carefully assessed for skin and retinal lesions.
- CT or MRI will confirm the diagnosis.
- Genetic testing is available for mutations in TSC1 and TSC2.

SLEEP DISORDERS

Parasomnias

- As a group, these disorders are:
  - Paroxysmal.
  - Predictable in their appearance in the sleep cycle.
  - Nonresponsive to environmental manipulation .
  - Characterized by retrograde amnesia.
  - A thorough history makes the diagnosis and an extensive workup is rarely needed.

NIGHT TERRORS (PAVOR NOCTURNAS)

DEFINITION

- Transient, sudden-onset episodes of terror in which the child cannot be consoled and is unaware of the surroundings, usually lasting for 5–15 minutes.
- There is total amnesia following the episodes.

EPIDEMIOLOGY

Occur in 1–3% of the population, primarily in boys between ages 5 and 7.

PATHOPHYSIOLOGY

- Fifty percent complete recovery by age 8.
- Fifty percent are also sleepwalkers.
- Often, incontinence and diaphoresis.
- Occur in stage 4 (deep) sleep, which is first third of night sleep.

DIAGNOSIS

PSG (polysomnography).

TREATMENT

Reassurance; usually self-limited and resolve by age 6.

SOMNAMBULANCE (SLEEPWALKING)

- Occurs during slow-wave sleep.
- Occurs during first third of the night.
- Onset: 8–12 years.
- Awakened only with difficulty and may be confused when awakened.
- Fifty percent also have night terrors.

NIGHT TERRORS	NIGHTMARES
NREM sleep	REM sleep
No memory of the event; goes back to sleep	Remembers dream and afraid to sleep
2 hours after falling sleep (first third of sleep)	Close to morning (last third of sleep)
Disappears by age 6	Peak 3–6 years; less frequent in adolescent
Sleepwalking common	No sleepwalking

INSOMNIA

- Affects 10–20% of adolescents.
- Depression is a common cause and should be ruled out.

OBSTRUCTIVE SLEEP APNEA (OSA)

- Occurs in 2–5 % of children, most often between ages 2 and 6.
- Characterized by chronic partial airway obstruction with intermittent episodes of complete obstruction during sleep, resulting in disturbed sleep.
- Snoring is the most common symptom, occurring in most of them (12% of general pediatric population has snoring without OSA).
- **Symptoms:** Fatigue/hyperactivity, headache, daytime somnolence.
- **Signs:** Narrow airway, tonsillar hypertrophy, often obese.
- **Diagnosis:** History and physical examination, polysomnography (>1 apnea/hypopnea per hour).

EXAM TIP

Night terrors, sleepwalking, and nightmares are associated with disturbed sleep, but have no known neurologic disorder.

WARD TIP

Sleep deprivation causes attention deficit, hyperactivity, and behavior disturbances in children—often mistaken for attention deficit/hyperactivity disorder (ADHD).

WARD TIP

Obstructive sleep apnea due to adenotonsillar hyperplasia is an indication for tonsillectomy and adenoidectomy.

EXAM TIP

Since obstructive sleep apnea causes hypoxia, it may be associated with polycythemia vera, growth failure, and serious cardiorespiratory pathophysiology.

Coma

- Consciousness refers to the state of awareness of self and environment.
- Pediatric evaluation of consciousness is dependent on both age and developmental level.

DEFINITION

Pathologic cause of loss of normal consciousness.

PATHOPHYSIOLOGY

- Consciousness is the result of communication between the cerebral cortex and the ascending reticular-activating system.
- Coma can be caused by:
  - Lesions of the medullary reticular-activating system or its ascending projections. Ventral pontine lesions → locked-in syndrome, which is not coma.

ETIOLOGY

- Structural causes include trauma, vascular conditions, and mass lesions involving directly or mass effects.
- Metabolic and toxic causes include hypoxic-ischemic injury, toxins, infectious causes, and seizures.

EVALUATION

- Administer glucose via IV line so that the brain has an adequate energy supply.
- Treat underlying cause (toxin antidote, reduce ICP, antibiotics, etc.).

PROGNOSIS

- Overall, children tend to do better than adults.
- Several measurement scales have been published attempting to predict outcome. The most widely accepted is the Glasgow Coma Scale (see Table 17-5).
- Another scale that you should know exists is the Pediatric Cerebral Performance Category Scale, which, unlike the Glasgow, was specifically designed for pediatric patients.

> **WARD TIP**
>
> Herniation is a result of increased intracranial pressure and often leads to coma or death.
>
> **Herniation syndromes that may result in coma:**
> - **Uncal herniation:** Pressure on CN 6 with diploplia and inability to abduct eye
> - **Central (trans-tentorial herniation):** Blown (fixed and dilated) pupil, ptosis, CN 3 compression (down and out eye), ipsilateral hemiplegia

> **WARD TIP**
>
> Prognosis depends on the etiology of the insult and the rapid initiation of treatment!

ENCEPHALOPATHIES

CNS Infection

MENINGITIS

DEFINITION

- Diffuse inflammation of the meninges, particularly arachnoids and pia mater.
- **Bacteria:**
  - <3 months: Group B streptococci and gram-negative organisms, *Escherichia coli, Listeria.*

TABLE 17-5.   **Glasgow Coma Scale (GCS)**

EYE OPENING (TOTAL POINTS: 4)	
Spontaneous	4
To Voice	3
To Pain	2
None	1

VERBAL RESPONSE (TOTAL POINTS: 5)			
INFANTS AND YOUNG CHILDREN		**OLDER CHILDREN**	
Appropriate words; smiles, fixes, and follows	5	Oriented	5
Consolable crying	4	Confused	4
Persistently irritable	3	Inappropriate	3
Restless, agitated	2	Incomprehensible	2
None	1	None	1

MOTOR RESPONSE (TOTAL POINTS: 6)	
Obeys	6
Localizes pain	5
Withdraws	4
Flexion	3
Extension	2
None	1

Note minimum score is 3, not 0.

- >3 months: *Streptococcus pneumoniae, Haemophilus influenzae* type b, and *Neisseria meningitidis* (two life-threatening clinical syndromes: meningococcemia and meningococcal meningitis).
- **Virus:** The term *aseptic meningitis* is used to describe the syndrome of meningism and CSF leukocytosis usually caused by viruses or bacteria.

SIGNS AND SYMPTOMS

If immunocompromised, these signs and symptoms will be not prominent.
- Fever, headache, and nuchal rigidity (most important features).
- Photophobia or myalgia may be present.
- Meningism (Brudzinski and Kernig signs) (see Figures 17-5 and 17-6).
- Altered consciousness, petechial rash, seizures, cranial nerve, or other abnormal neurological findings.
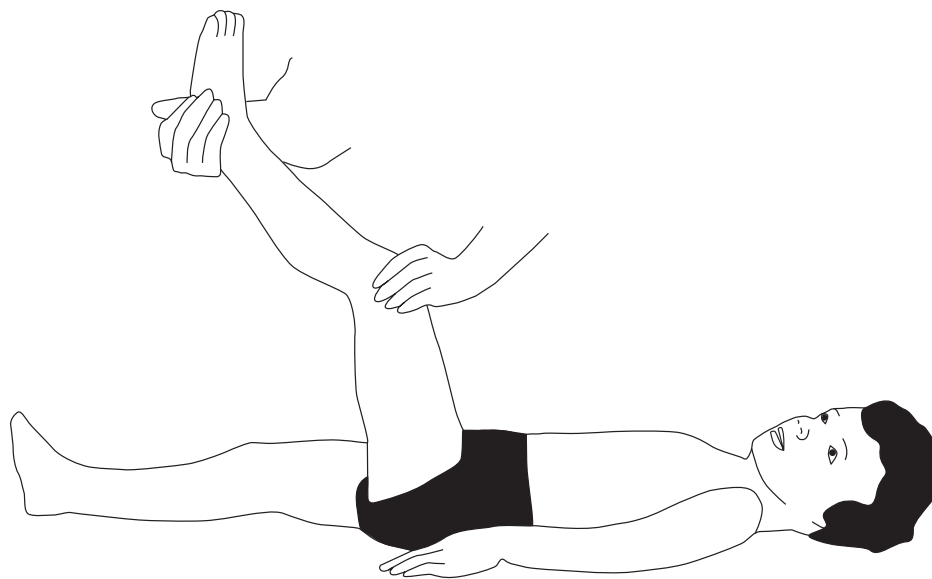
FIGURE 17-5. **Kernig sign.** Flex patient's leg at both hip and knee, and then straighten knee. Pain on extension is a positive sign.
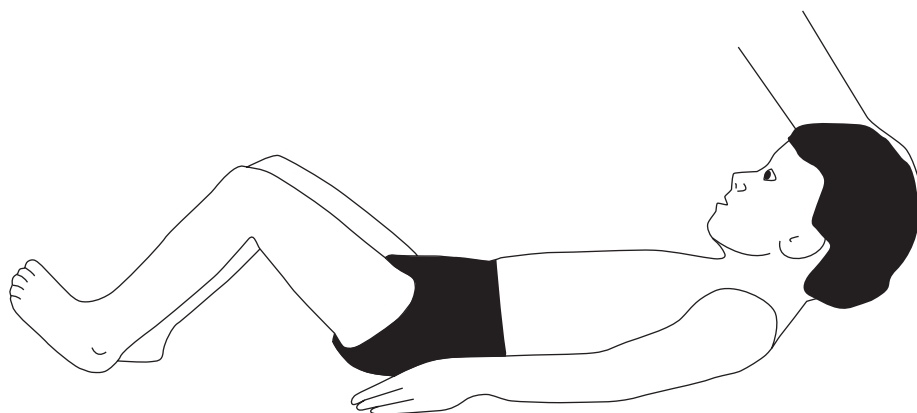
FIGURE 17-6. **Brudzinski sign.** Involuntary flexion of the hips and knees with passive flexion of the neck while supine.

DIAGNOSIS

Analysis of the CSF is not always predictive of viral or bacterial infection since there is considerable overlap in the respective CSF findings, especially at the onset of the disease (Table 17-6).

Bacterial Meningitis

- See Table 17-7 for common meningitis-causing bacteria.
- Associated with high rate of complications and chronic morbidity and death.
- Pathogenesis: 95% blood-borne. Organism enters the CSF, multiplies, and stimulates an inflammatory response. Direct toxin from organism, hypotension, or vasculitis → thrombotic event; vasogenic/cytotoxic edema causes ↑ ICP and ↓ blood flow, which all may contribute to further damage.

Viral Meningitis

- Enterovirus (85%): Echovirus, coxsackievirus, and nonparalytic poliovirus.
- Other classic causes are herpes simplex virus type 1 (HSV-1), Epstein-Barr virus (EBV), mumps, influenza, arboviruses, and adenoviruses.

EXAM TIP

Take some time to familiarize yourself with Tables 17-6 and 17-7: *You will be asked this!*

EXAM TIP

Chronic meningitis: Subacute symptoms of meningitis for >4 weeks: Infectious, autoimmune, or neoplastic.

TABLE 17-6. Cerebrospinal Fluid (CSF) Findings in Meningitis

	NORMAL LEVELS	BACTERIAL	VIRAL	FUNGAL	TB
Appearance		Turbid	Clear	Clear	Fibrinous
Cells	Mononuclear	Polymorphs	Mononuclear	Mononuclear	Mononuclear
Leukocytes (mm³)	< 5	100–1000	50–1000	> 100	100–500
Protein (mg/dL)	20–45	100–500	50–200	25–500	1–5 g/dL
Glucose (mg/dL)	> 50 or 75% serum glucose	↓ < 40 or 66% serum	Generally normal	< 50; continues to decline if untreated	Less than half of the serum
Lab cultures		■ Gram stain of CSF	■ Hard to detect ■ PCR of CSF may show HSV or enteroviruses	■ Budding yeast may be seen ■ Cryptococcal antigen may be positive in serum and CSF	Ziehl Neelsen AFB stain PCR

CSF, cerebrospinal fluid; PCR, polymerase chain reaction; HSV, herpes simplex virus.

TABLE 17-7. Common Causes of Pediatric Bacterial Meningitis

AGE	BACTERIA	TREATMENT
Neonates (< 1 month)	Group B streptococcus	Ampicillin and a third-generation cephalosporin
	Gram-negative enteric bacilli	
	Listeria monocytogenes	
	Escherichia coli	
Infants (1–24 months) and children <10 yr	*Streptococcus pneumoniae*	Third-generation cephalosporin
	Neisseria meningitidis	Vancomycin should be added until susceptibility is known
	Haemophilus influenzae type B	
Children ages 10–19 yr	*Streptococcus pneumoniae*	Third-generation cephalosporin
	Neisseria meningitidis	Vancomycin should be added until susceptibility is known

- Clinical presentation is similar but symptoms usually are less severe than that of bacterial meningitis.
- Children may not be toxic appearing.
- Children show typical viral-type infectious signs (fever, malaise, myalgia, nausea, and rash) as well as meningeal signs.
- Typically is a self-limited process with complete recovery, and treatment is supportive.

Fungal Meningitis

- Although relatively uncommon, the classic organism is *Cryptococcus.*
- Encountered primarily in the immunocompromised patient (with transplants, AIDS, or on chemotherapy).
- May be rapidly fatal (as quickly as 2 weeks) or evolve over months to years.
- Tends to cause direct lymphatic obstruction, → hydrocephalus.

Treatment

- Third-generation cephalosporin (cefotaxime/ceftriaxone).
- Add ampicillin for *Listeria* in neonates. Neonates can be treated with ampicillin + gentamicin or ampicillin + cefotaxime.
- Add vancomycin, considering the increasing resistance of pneumococci to cephalosporins and carbapenems until the sensitivities are known.
- If viral etiology is suspected or CSF is not clearly differentiating between bacterial and viral etiologies, consider adding acyclovir until viral polymerase chain reaction (PCR) comes back negative.
- Steroid use is controversial.

Encephalitis

Definition

- A disease process in the brain primarily affecting the brain parenchyma.
- Because patients often have symptoms of both meningitis and encephalitis, the term *meningoencephalitis* is often applied.

Etiology

Chronic Bacterial Meningoencephalitis
1. *Mycobacterium tuberculosis, M. bovis,* and *M. avium-intracellulare.*
   - Nonspecific features develop over days to weeks. Patients have generalized complaints of headache, malaise, and weight loss initially.
   - This is followed by confusion, focal neurological signs, cranial nerve palsies, and seizures or, in advanced cases, hemiparesis, hemiplegia, or coma.
   - Serious complications include arachnoid fibrosis, → hydrocephalus, and arterial occlusion, → infarcts.
   - *M. avium-intracellulare* is common in AIDS patients.
2. Neurosyphilis (tabes dorsalis).
   - Causative organism is *Treponema pallidum.*
   - May present with aseptic meningitis only.
   - Tertiary syphilis (late-stage syphilis) manifests with neurologic, cardiovascular, and granulomatous lesions.
   - Congenital syphilis presents with a maculopapular rash, lymphadenopathy, and mucopurulent rhinitis.
   - Routine prenatal screening for syphilis is now mandatory in most states to prevent congenital syphilis.

Viral Meningoencephalitis
1. **Herpes simplex virus:**
   - HSV-1: Most cases after the neonatal period.
   - HSV-2: Usually blood-borne and results in diffuse meningoencephalitis and other organ involvement. It is the congenitally acquired form, transmitted to 50% of babies born to a mother with active vaginal lesions.

2. **Herpes zoster virus:**
   - Can occur after primary infection or as a result of reactivation later in life.
   - Usually with a rash, but outcome is poor in those without a rash.
   - In immunocompetent hosts, after 2–6 months of primary infection, the dormant virus in the ganglia becomes activated in and causes large-vessel vasculitis → infarcts.
   - In immunocompromised hosts, the dormant virus causes small-vessel vasculitis and results in hemorrhagic infarcts of gray and white matter.
   - EEG will show diffuse slowing and periodic lateralizing epileptiform discharges (PLEDs).
3. **Rabies:**
   - Causes severe encephalitis, coma, and death due to respiratory failure.
   - Transmitted via bite or saliva from an infected animal, usually associated with dogs, bats, skunks, raccoons, or squirrels.
   - The virus travels up the peripheral nerves from the bite site and enters the brain.
   - Nonspecific symptoms (fever, malaise) and paresthesia around the bite site are pathognomonic. This is followed by more specific neurologic symptoms of hydrophobia, aerophobia, agitation, **hypersalivation,** and seizures. This proceeds to coma and death.
   - Prophylaxis is indicated when there is potential exposure with rabies immunoglobulin and rabies vaccine (multiple doses).

Transverse Myelitis

DEFINITION

- An acute focal infectious or immune-mediated illness causing swelling and demyelination of the spinal cord. This most commonly affects the thoracic spinal cord (80%) followed by cervical cord.
- It is a neurological emergency and requires prompt diagnosis and treatment to prevent permanent damage.

SIGNS AND SYMPTOMS

- Fever, lethargy, malaise, muscle pains.
- Begins acutely and progresses within 1–2 days.
- Back pain at the level of the involved cord and paresthesias of the legs are common.
- Anterior horn involvement may cause lower motor neuron dysfunction.
- Bladder and bowel dysfunction is present.

DIAGNOSIS

- MRI: Enhanced T2 signals.
- CSF: Pleocytosis.
- Electromyogram (EMG): Anterior horn-cell dysfunction in involved segments.

TREATMENT

IV steroids, intravenous immune globulin (IVIG), may require surgical intervention.

PROGNOSIS

Most make good recovery; however, it is slow.

Acute Disseminated Encephalomyelitis (ADEM)

DEFINITION

- An immune-mediated demyelinating encephalopathy in which there is a sudden widespread attack of the inflammation of the brain, spinal cord, and nerves, with destruction of white matter.
- Two-thirds with history of an antecedent viral infection.
- Some features resemble multiple sclerosis.

SIGNS AND SYMPTOMS

- Abrupt onset of change in consciousness or behavior changes unexplained by fever.
- Often associated with at least one fever free day before onset of symptoms.
- Irritability and lethargy are common first signs of acute disseminated encephalomyelitis.
- Fever returns and headache are present in up to half of the cases. Meningismus is also detected in approximately one-third of the cases. Over the course of minutes to weeks, multifocal neurologic abnormalities develop which can include weakness, ataxia, and cranial nerve abnormalities.

DIAGNOSIS

MRI: ADEM lesions are characteristically multiple, bilateral but asymmetric, and widespread within the CNS.

TREATMENT

First-line high-dose IV steroids, also intravenous immune globulin (IVIG).

PROGNOSIS

2–10% mortality but most recover completely or with mild sequelae.

WARD TIP

ADEM is associated with bilateral optic neuritis and MS is usually unilateral.

Tetanus

A 1-week-old child born to an immunocompromised mother presents with difficulty feeding, trismus, and other rigid muscles. *Think: Tetanus.*
Tetanus is a toxin-mediated disease characterized by severe skeletal muscle spasms. It is a serious infection in neonatal life. Initial symptoms can be nonspecific. Inability to suck and difficulty in swallowing are important clinical features followed by stiffness and seizures. Neonatal tetanus can be prevented by immunizing mothers before or during pregnancy and providing sterile care throughout the delivery.

DEFINITION

- An acute illness with painful muscle spasms and hypertonia caused by the neurotoxin produced by *Clostridium tetani*.
- These symptoms usually start in the jaw and facial muscles and progressively involve other muscle groups.

SIGNS AND SYMPTOMS

- Trismus (masseter muscle spasm) is the characteristic sign and is present in 75% of cases.
- **Risus sardonicus,** a grin caused by facial spasm, is also classic.
- Dysphagia due to pharyngeal spasm develops over a few days; laryngospasm may result in asphyxia.
- Descending paralysis and when involves the trunk and thigh, the patient may exhibit an arched posture in which only the head and heels touch the ground.
- Late stages manifest with recurrent seizures consisting of sudden severe tonic contractions of the muscles with fist clenching, flexion, and adduction of the upper limb and extension of the lower limb and is associated with poor prognosis.
- Autonomic dysfunction may be seen as ↑ sweating, heart rate, blood pressure, and temperature.
- Can also present with localized spasms at the site of infection or with abdominal pain mimicking acute abdomen.
- Incubation period varies from 2 to 14 days (average 7 days).

DIAGNOSIS

- Diagnosis is clinical: Trismus, dysphagia, ↑ rigidity, and muscle spasms.
- Laboratory studies are usually normal, but a moderate leukocytosis may be present.
- CSF is normal.
- Gram stain is positive in only one-third of the cases.

TREATMENT

- Prophylactic intubation.
- Rapid administration of human tetanus immune globulin.
- IV penicillin G, metronidazole, or doxycycline.
- Surgical excision and debridement of the wound.
- Muscle relaxants such as diazepam and phenobarbital should be used to promote relaxation and seizure control. Neuromuscular blocking agents like vecuronium are also used.

PROGNOSIS

- Mortality rate: 5–35%.
- Neonatal tetanus mortality ranges from 10% to 75%, depending on quality of care received.

WARD TIP

Tetanic contractions can be triggered by minor stimuli, such as a flashing light. Patients should be sedated, intubated, and put in a dark room in severe cases.

EXAM TIP

Tetanus is an entirely preventable disease via immunization.

Other Encephalopathies

ANTI-NMDA RECEPTOR ENCEPHALITIS

BACKGROUND

- An acute form of encephalitis that is potentially lethal but has a high probability for recovery with treatment.
- Autoimmune reaction, antibodies against NR1-NR2 NMDA receptors (N-methyl-D-aspartate receptor).
- Often associated with tumors, classically ovarian teratomas, but many have no tumor association.

SIGNS AND SYMPTOMS

- Abrupt onset of change in consciousness or behavior changes unexplained by fever.
- Initially, symptoms are nonspecific including fever, headache, and fatigue.
- This is followed by a stage of psychosis with agitation, paranoia, psychosis, and violent behaviors and can be associated with bizarre behavior, hallucinations.
- Symptoms can progress to altered level of consciousness, hypoventilation, seizures, autonomic instability, and dyskinesias.

DIAGNOSIS

- Serum NMDA-receptor antibodies in the CSF.
- Pelvic ultrasound to rule out tumor.
- Exclude other causes of encephalopathy.

TREATMENT

- Early removal of tumor if present.
- IV corticosteroids, IVIG, and plasma exchange therapy in severe cases.

PROGNOSIS

- The recovery process from anti-NMDA encephalitis can take many months.
- ~50% will fully recover. Some will recover with variable sequelae or deficits. <10% mortality.

> **EXAM TIP**
>
> The diagnosis of anti-NMDA receptor encephalitis is often delayed due to resemblance to other conditions, particularly psychiatric disorders.

MITOCHONDRIAL ENCEPHALOPATHY

A group of disorders that can be caused by mutations in either nuclear or mitochondrial DNA, resulting in a variety of symptoms:

1. **Mitochondrial encephalopathy, lactic acidosis, and strokelike episodes (MELAS):**
   - The most common of mitochondrial encephalopathies.
   - Onset between ages 2 and 10 years; initial development normal, but short stature is present.
   - The most initial feature is GTC seizure (often associated with hemiparesis and cortical blindness), recurrent headache, and vomiting.
   - The neurologic abnormalities are transient initially, but later become progressive and → coma and death.
   - MRI shows multiple strokes not in vascular distribution pattern. ↑ lactic acid in blood and CSF. Muscle biopsy is diagnostic (ragged-red fibers).
2. **Myoclonic epilepsy with ragged-red fibers (MERRF):**
   - Onset may be in childhood or adult life.
   - Four cardinal features are myoclonus, myoclonic epilepsy, ataxia, and ragged-red fibers on muscle biopsy.
   - The initial feature is progressive insidious decline in school performance. GTC seizures or myoclonus is usually the first symptom to seek medical attention. Later, they develop progressive epilepsy, cerebellar ataxia, and dysarthria. Clinical myopathy may not be present.
   - Diagnosis is by gene testing and muscle biopsy.
3. **Reye syndrome:**
- A disorder of mitochondrial dysfunction associated with viral infection and aspirin ingestion.
- Sporadic syndrome can occur with varicella-zoster or influenza B infection.

> **EXAM TIP**
>
> MELAS and MERRF are caused by point mutations in transfer RNA (tRNA) in mitochondrial DNA.
> - MELAS = leucine
> - MERRF = lycine
> - MERRF is often confused with Friedreich ataxia

- Recurrent Reye-like syndrome is seen in children with inborn errors of metabolism, medium-chain acyl Co-A dehydrogenase (MCAD) deficiency, urea cycle disorders, pyruvate metabolism disorders.
- **Diagnosis:** Liver biopsy is diagnostic. ↓ blood glucose, ↑ ammonia and liver enzymes without jaundice.

HEPATIC ENCEPHALOPATHY

- Acute hepatic failure caused by viral hepatitis, drugs, toxins, or Reye syndrome results in altered consciousness (due to cerebral edema and accumulation of toxins, ammonia).
- In children, most commonly related to fulminant viral hepatitis (50–75%).
- Early symptoms are malaise, lethargy, jaundice, dark urine, and abnormal liver function tests (LFTs). The encephalopathy can be acute or chronic.
- Other features include sleep disturbance, change in affect, drowsiness, asterixis (flapping tremor). Decerebrate posturing may occur in the terminal stages.
- Hepatic encephalopathy is reversible with treatment, and most therapies are aimed at controlling the cerebral, renal, and cardiovascular functions until the liver regenerates or liver transplantation can be done. These are achieved by lowering:
  - Ammonia level (↓ dietary protein, stop gastrointestinal [GI] bleed, treat constipation).
  - Cerebral edema with fluid restriction and the use of hyperosmolar agents (mannitol).
- Patients who recover typically have no long-term sequelae.

HIV/AIDS ENCEPHALOPATHY

- There is a 40–90% incidence of CNS involvement in perinatally infected children.
- Ninety percent of infected infants are symptomatic by 18 months of age.
- Develops 2–5 months after infection.
- Commonly presents with progressive encephalopathy and hepatosplenomegaly, → failure to meet developmental milestones, impaired brain growth, and symmetrical motor dysfunction.
- Imaging techniques reveal cerebral atrophy in 85% of children and ventricular enlargement.
- Basal ganglia calcifications may be present.
- Opportunistic infections such as toxoplasmosis typically occur later in adolescence.
- PCR analysis of HIV DNA or RNA is used to detect HIV infection in infants <18 months.
- **Diagnosis:** Via immunoglobulin G (IgG) antibody to HIV for patients >18 months and a confirmatory test HIV DNA PCR.
- **Treatment:** Highly active antiretroviral therapy (HAART).
- All pregnant mothers are tested for HIV infection and are treated to ↓ the transmission.

ADRENOLEUKODYSTROPHY

- A progressive disease, characterized by demyelination of the CNS and peripheral nerves and adrenal insufficiency.
- X-linked recessive, peroxisomal disorder, defect in the ability to catabolize long-chain fatty acids (LCFAs).

- It presents between 4 and 10 years with behavioral and cognitive decline with visual loss, followed by motor symptoms.
- **Diagnosis:** White matter abnormality on MRI, ↑ serum very-long-chain fatty acids (VLCFA), labs for adrenal insufficiency.
- **Treatment:** Bone marrow transplantation if only radiological changes are present and no appearance of the neurological symptoms.

LEAD ENCEPHALOPATHY

- There is no direct correlation to the level of lead and clinical manifestations. Blood lead level >5 µg/dL is considered toxic. Lead interferes with porphyrin metabolism in red blood cells (RBCs).
- **Acute:** Vomiting, abdominal pain, seizures, impaired consciousness, and respiratory arrest are common.
- **Chronic:** Gradual confusion, behavior changes, sleep problems, seizures, ataxia. Peripheral neuropathy, while common in adults, is rarely seen in children unless they also have sickle cell anemia.
- Pica is common in these children (e.g., eating paint chips).
- Diagnosis is made primarily through history and also via blood lead testing. Microcytic hypochromic anemia, basophilic stippling, and azotemia also present.
- Treatment: Removing the source of lead, and chelation therapy when blood lead level >45 µg/dL.

Movement disorders

Can be classified by a paucity of movement (hypokinetic) versus excessive or exaggerated movement (hyperkinetic). Hyperkinetic movement disorders predominate in children.

SYDENHAM'S CHOREA

- Most frequent cause of new onset chorea in children.
- Rapid, brief, unsustained, nonstereotypical movements of the body.
- Autoimmune mediated.
- Twice as common in females.
- Onset: Age 3–17 years.
- Postinfectious chorea appearing 4–8 weeks after a group A streptococcal pharyngitis.
- Resolves after 8–9 months; 50% have persistent chorea.
- **Diagnosis:** Recent throat infection (anti-streptolysin O, DNase B), ↑ T2 signals in basal ganglia.
- **Treatment:**
    - Valproate: First choice.
    - Dopamine-blocking agents: Second choice.
    - Also treat primary infection.

TOURETTE SYNDROME

- A lifelong condition affecting 1 in 2000 that presents before age 15.
- Diagnostic criteria: Multiple motor and vocal tics for >1 year with tic-free period not more than 3 consecutive months.

- Often associated with other conditions like obsessive-compulsive disorder (OCD), attention deficit/hyperactivity disorder (ADHD).
- Symptoms are enhanced by stress and anxiety.
- Treatment with medications should be avoided.
- Treat when tics interfere with child's developmental learning or cause undue social stress. Also treat comorbid conditions.

PANS AND PANDAS

- PANS (Pediatric Acute-onset Neuropyschiatric Syndrome) and PANDAS (Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococci) have nearly identical presentations.
- PANS is associated with a variety of infections and PANDAS is always associated with streptococci.
- Manifested by the development or exacerbation of tics and/or obsessive-compulsive disorder (OCD).
- Diagnosis is considered controversial by some authorities.

Ataxias

Inability to coordinate muscle activities to regulate posture and also strength and direction of extremity movements (see Table 17-8).

EXAM TIP

Titubations are a disturbance of body equilibrium in standing or walking, resulting in an uncertain gait and trembling, especially resulting from diseases of the cerebellum.

TYPES

Acute Cerebellar Ataxia

- A diagnosis of exclusion occurring in children 2–7 years old.
- Often follows viral infection by 2–3 weeks; thought to be autoimmune response and has been seen with live inactivated vaccines like varicella vaccine.

TABLE 17-8. Ataxias

TYPE	COMMON FEATURES	EXAMPLES
Sensory	Gait: Wide based and high stepping Falls in dark or eyes closed (Romberg +) Difficulty of fine finger movements	Posterior column involvements like B_{12} deficiency
Cerebellar	Gait: Wide based and crunchy so cannot perform Romberg test. Intention tremors, nystagmus, dysmetria, titubations, hypotonia	Spinocerebellar ataxia Pontocerebellar hypoplasia Vermian agenesis or dysgenesis Cerebellar degeneration in trisomies, etc.
Mixed	Both sensory and cerebellar components	Friedreich ataxia Vincristine side affect

- Sudden onset of severe truncal ataxia; often, the child cannot stand or sit.
- Severity is maximum at the onset with clear sensorium.
- Horizontal nystagmus in 50%.
- **Diagnosis:** Diagnosis of exclusion; exclude other serious causes first.
- **Treatment:** Self-limited disease.
- **Prognosis:** Complete recovery typically occurs within 2 months (1–5 months).

Freidreich's Ataxia

- Autosomal-recessive mutation (usually a triplet expansion) in Frataxin gene on chromosome 9.
- Degeneration of the dorsal columns and rootlets, spinocerebellar tracts, and, to a lesser extent, the pyramidal tracts and cerebellar hemispheres.
- Onset before age 10 (2–16 years).
- Slow progression of ataxia involving the lower limbs > upper limbs associated with dysarthria, ↓ tendon reflexes, positive Babinski sign, high-arch foot with loss of dorsal column sensations.
- Romberg test is positive.
- Associated abnormalities include skeletal abnormalities (scoliosis), cardiomyopathy, and optic atrophy.
- Elevated α-fetoprotein (AFP).
- Clinical features establish the diagnosis, which is confirmed with genetic testing. There is no curative treatment available but symptomatic treatment to improve quality of life.

Ataxia-Telangiectasia

- Autosomal-recessive disorder of nervous and immune system due to gene mutation at chromosome 11.
- The most common degenerative ataxia.
- A slowly progressive ataxia beginning during first year of life resulting in inability to walk by adolescence.
- Oculomotor apraxia is present in 90% of the patients.
- Telangiectasia becomes evident after 2 years or in the teenage years and is most prominent on the bulbar conjunctiva (first), bridge of nose, and exposed surfaces of the extremities. Sun exposure exacerbates the telangiectasia.
- Sinopulmonary infection is another important feature. ↓ or absent IgA, IgE, and especially IgG_2 subclass. IgM may be increased.
- ↑ AFP and peripheral acanthocytes.
- Have a 50- to 100-fold greater chance of brain tumors and lymphoid tumors, so avoid radiation exposure by limiting imaging studies.

Peripheral Neuropathies

- Injuries to the peripheral nerves may be either:
    - Demyelinating (injury to Schwann cells).
    - Degenerating (injury to the nerve or axon).
- Peripheral neuropathy is the most common cause of progressive distal weakness.
- Most common are hereditary causes and slow progression.
- The most common acquired cause is Guillain-Barré syndrome (GBS) with rapid progression.

WARD TIP

Myoclonic epilepsy with ragged-red fibers (MERRF) is often confused with Friedreich ataxia.

Guillain-Barré Syndrome

A 6-year-old boy with no significant past medical history presents to the ED with difficulty walking for past few days and is now unable to walk. He also has some weakness in his upper extremities but he does not have any respiratory distress. There is no clear history of any recent illness, vaccination, or sick contacts. He had upper respiratory infection symptoms a few weeks ago. On examination, he is weaker more in the lower extremities than upper, and deep tendon reflexes are absent at knee and ankle. *Think: Guillain-Barré syndrome (GBS).*

GBS is an ascending paralysis. History of prior upper respiratory tract or viral infection or recent vaccination may be present. Initial symptoms are pain, numbness, paresthesia, or weakness in the lower extremities, which rapidly progresses to bilateral and relatively symmetric weakness. ↓ or absent deep-tendon reflexes are often present. Lumbar puncture typically shows ↑ protein with normal CSF and white cell count (cytoalbuminologic dissociation).

- A postinfection demyelinating neuropathy affecting predominantly the motor neurons.
- It is due to immune cross-reactivity to a secondary illness within 4 weeks. Most commonly seen after upper respiratory infection (URI), *Campylobacter jejuni*, *Mycoplasma pneumoniae*, cytomegalovirus (CMV), Epstein-Barr virus (EBV), varicella, influenza, hepatitis A and B infection.
- Weakness begins in the legs and progresses symmetrically upward to the trunk, arms, then bulbar and ocular muscles.
- Tendon reflexes are absent.
- Respiratory muscles in 50%, autonomic dysfunction, pain, paresthesias can be present.
- ↑ proteins in CSF with no ↑ in lymphocytes.
- Nerve conduction will be slow with conduction blocks, and enhancement of nerve roots can be seen on MRI.
- Treatment includes close monitoring for respiratory weakness and IVIG or plasmapheresis in more severe cases.

Botulism

- Botulinum toxin is disseminated through the blood and, due to the rich vascular network in the bulbar region, symmetric flaccid paralysis of the cranial nerves is the typical manifestation.
- Infant botulism: The first sign is usually absence of defecation. The head control is lost and the weakness descends.
- Most dreaded complication is respiratory paralysis, and approximately 50% of patients are intubated.
- Prognosis is good in noncomplicated cases.
- Antibiotics and blocking antibodies have not been shown to affect the course of the disease.
- Electromyogram (EMG) with high frequency (20–50 Hz) reverses the presynaptic blockade and produces an incremental response.

Myasthenia Gravis

- ↓ in postsynaptic acetylcholine receptors due to autoimmune degradation, resulting in rapid fatigability of muscles.
- Ptosis and extraocular eye weakness are the earliest and most diagnostic symptoms.

EXAM TIP

It is not possible to have botulism without having multiple cranial nerve palsies.

EXAM TIP

Infantile botulism traditionally associated with ingestion of honey (honey contains botulism spores) which is why honey is not given in the first year of life. Most cases are due to ingestion of environmental dust or soil from home canned foods or construction at or near the home.

- Onset usually after age 8, as early as 6 months. Prepubertal male bias, postpubertal female bias.
- Diagnosis is made by EMG with repetitive stimulation, edrophonium (Tensilon) test, a quick test (acetylcholinesterase inhibitor). Acetylcholine receptor-binding or receptor-blocking antibodies are detected in the sero-positive forms and are an indication for thymectomy. May be associated with autoimmune thyroid disease and seizures.
- Cholinesterase drugs are the mainstay of treatment, with oral steroids used as needed for immune suppression (initially may exacerbate the disease).
- Prognosis varies, with some children undergoing spontaneous remission, while in others the disease persists into adulthood.

Transitory Neonatal Myasthenia

- Passive transfer of antibodies from myasthenic mothers (10–15% incidence).
- Self-limited disease consisting of generalized weakness and hypotonia for 1 week to 2 months. Symptoms develop a few hours after birth. If develop after 3 days, then are unlikely.
- Poor suck and respiratory problems are addressed with supportive care. Neostigmine or exchange transfusion can be used in more severe cases.

Electrolyte Imbalances

See Table 17-9 for common electrolyte imbalances affecting the nervous system.

TABLE 17-9. Electrolyte Disturbances and the Nervous System

DISTURBANCE	MANIFESTATION	COMMON CAUSES
Hyponatremia	■ Rapid onset: Brain swelling, lethargy, coma, and seizures ■ Slow onset: Usually asymptomatic	■ Typically impaired renal water excretion in the presence of normal water intake
Hypernatremia	■ Intracranial bleeding is common in children (dehydrated brain shrinks and can tear bridging veins)	■ Most common cause is dehydration or inadequate intake of water ■ Rare
Hypokalemia	■ Neuromuscular: Weakness, paralysis, rhabdomyolysis ■ Gastrointestinal: Constipation, ileus ■ Nephrogenic diabetes insipidus ■ ECG changes: Prominent U waves, T-wave flattening ■ Arrhythmias	■ Uptake into cells ■ Renal loss ■ Severe diarrhea, laxative abuse ■ Magnesium depletion is an important and often overlooked cause
Hyperkalemia	■ Severe cases are a medical emergency! ■ Neuromuscular: Weakness, ascending paralysis, respiratory failure ■ Progressive ECG changes with increasing potassium: 　■ Peaked T waves 　■ Flattened P waves 　■ Long PR interval 　■ Idioventricular rhythm 　■ Wide QRS and deep S waves 　■ Sine-wave pattern and ventricular fibrillation	■ Shift out of cells ■ Aldosterone deficiency/unresponsiveness ■ Renal failure

Headaches

MIGRAINE

The most common type of headache in the pediatric population with female predominance.

DEFINITION

A recurrent headache with symptom-free intervals and can be associated with the following:
- Abdominal pain.
- Nausea and/or vomiting.
- Throbbing headache.
- Often bilateral (versus unilateral in adults).
- Associated aura.
- Relieved by sleep.
- Family history of migraines.

Diagnosis of migraine is clinical and no neuroimaging is necessary unless it is persistently occipital or with abnormal neurologic examination.

CLASSIFICATION

Migraines may be classified into the following subgroups:

Migraine without Aura

- Headache lasting 4–72 hours.
- Two of the following: Unilateral, pulsating, moderate/severe pain, aggravation of routine physical activity.
- Headache may have associated nausea, vomiting, photophobia, phonophobia.

Migraine with Aura

- Headache with fully reversible aura symptoms:
- Visual, sensory, speech, motor, brainstem, retinal.
- Aura is accompanied or followed by headache within 60 minutes, and may last 5–60 minutes.
- Aura symptoms may spread gradually or two or more symptoms occur in succession.

Chronic Migraine

- Defined as headache on >15 days per month for more than 3 months.
- Daily headaches of less severity with less prominent migrainous features.

Complicated Migraine

Transient neurologic signs develop during a headache and persist after the resolution of the headache for a few hours to days.

TREATMENT

- Avoid the possible triggers: Often, migraines occur in response to specific triggers, such as psychological stress, strenuous exercise, sleep deprivation, cheese, chocolate, processed meat, or moving vehicles, and minimizing these factors may have great therapeutic effect.
- Consider nonpharmacologic treatment with biofeedback techniques in chronic stress headache.

WARD TIP

Episodic syndromes that may be associated with migraines include cyclic vomiting syndrome, abdominal migraine, benign paroxysmal vertigo, and benign paroxysmal torticollis.

- For acute attacks:
  - Dark, quiet environment and sleep.
  - Adequate fluid intake.
  - Pharmacologic therapy: Acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs) are first line.
  - Second-line drugs include triptans, caffeine, and ergot alkaloids (status migrinosus).
  - Antiemetics are helpful at the start of headache.
  - Treatment should be instituted as early as possible in an attack.

PROPHYLAXIS

- Antiepileptic drugs, such as topiramate, valproate, levetiracetam.
- Tricyclic antidepressants such as amitriptyline.
- β-blockers such as propranolol.

CLUSTER HEADACHE

- Brief, severe, unilateral stabbing headaches that occur multiple times daily over a period of several weeks and tend to be seasonal.
- Onset after 10 years of age.
- Male predominance.
- Conjunctival injection, tearing, rhinorrhea.
- Prophylaxis with lithium or calcium channel blocker.
- Acute treatment with 100% oxygen or sumatriptan and dihydroergotamine (DHE).

TENSION HEADACHE

Tension or stress headaches are rare in children prior to puberty and are often difficult to differentiate from migraines.

PRESENTATION

- Most often occur with a stressful situation, such as an exam.
- Described as "hurting" but not "throbbing."
- It presents like a band around the head. It is present most of the times of the day.
- Unlike migraines and ↑ intracranial pressure, tension headaches are not associated with nausea and vomiting.
- However, it is sometimes difficult to differentiate them from migraine.

DIAGNOSIS

- Diagnosis of exclusion.
- EEG or CT is not necessary.

TREATMENT

Steps should be taken to minimize anxiety and stress:
- Mild analgesics often are ample.
- Other options include counseling and biofeedback.
- Sedatives or antidepressants are rarely necessary.

INCREASED INTRACRANIAL PRESSURE (ICP)

Headache due to tension of the blood vessels or dura may be the first symptom of an ↑ in intracranial pressure.

WARD TIP

Prophylaxis should be offered to children with two or more migraines per month that interfere with activities such as school or recreation.

WARD TIP

Headaches can occur in children secondary to refractive errors. It is therefore imperative to perform a visual acuity determination.

WARD TIP

Normal ICP
Newborns: 6 mm Hg
Children: 6–13 mm Hg
Adolescents/adults: 0–15 mm Hg

SYMPTOMS

- It usually presents as headache, nausea, vomiting, diplopia, personality changes.
- It can present as bulging fontanelle, impaired upward gaze in infants.
- The presentation depends also on rate at which the ICP increases. If it increases slowly, then the intracranial structures have time to accommodate for the change.
- Coughing or Valsalva maneuver tends to make the pain worse by increasing ICP further.

ETIOLOGY

Common causes include posterior fossa brain tumors (and other brain tumors), obstructive hydrocephalus, hemorrhage, meningitis, venous sinus thrombosis, pseudotumor cerebri, abscesses, and chronic lead poisoning.

DIAGNOSIS

- Thorough history and physical exam are vital.
- Papilledema (if ↑ pressure is present for some time) and nuchal rigidity are helpful signs.
- Obtain CBC, erythrocyte sedimentation rate (ESR), and CT/MRI to narrow the differential.
- If CT/MRI is negative, consider lumbar puncture (LP).

TREATMENT

- Varies with particular diagnosis, and should be directed at the underlying etiology.
- Techniques to lower ICP acutely are as follows:
  1. Intubation and subsequent hyperventilation results in cerebral vasoconstriction, effective for about 30 minutes.
  2. Elevating the head 30 degrees facilitates venous return.
  3. Hyperosmolar agents such as mannitol (osmotic diuretic) or hypertonic 3% saline, avoid hypovolemia.
  4. Extraventricular drain provides temporary relief and can provide continuous monitoring of ICP.
  5. Surgical decompression if persistently remains ↑.

Aneurysms

- The pathogenesis of the aneurysms is multifactorial and controversial; however, it is believed that focal congenital weakness of the internal elastic lamina and muscular layers in the cerebral arteries → to aneurysmal formation.
- Most common in internal carotid artery followed by middle cerebral artery, anterior communicating artery, and basilar artery.
- Saccular aneurysms are the most common type and often at bifurcation of the internal carotid artery.
- Early warning signs are headaches or localized cranial nerve compression.
- Most common presentation is subarachnoid hemorrhage (SAH).
- More likely to rupture in patients <2 years of age or >10 years.
- More common in males 2:1.
- Familial occurrence is common.

ETIOLOGY

- Most often are related to congenital diseases:
  - Ehlers-Danlos syndrome.
  - Marfan syndrome, tuberous sclerosis.

WARD TIP

Any time you see papilledema, think ↑ ICP.

WARD TIP

Cushing triad: A sign of increased intracranial pressure and impending herniation of the brain
1. Irregular respirations
2. ↓ heart rate
3. ↑ BP (actually seen in 20–30%)

WARD TIP

Never perform an LP if papilledema is present. Must obtain CT before LP if suspicious of ↑ ICP.

- AVMs.
- Coarctation of the aorta.
- Polycystic kidney disease (likely develop secondary to hypertension in this condition); called **berry aneurysms.**
- Acquired aneurysms are most often related to bacterial endocarditis:
  - Embolization of bacteria results in mycotic aneurysms in the cerebral vasculature.
  - Twenty-five percent present with bleeding, such as a subarachnoid or intraparenchymal hemorrhage.

DIAGNOSIS

- Angiography is the gold standard for aneurysms in both children and adults.
- Magnetic resonance angiography (MRA) may also be used and is becoming more reliable.

TREATMENT

- Surgical clipping or endovascular coiling is the treatment of choice.
- Risk for rebleeding.

Arteriovenous Malformations (AVMs)

- True AVMs consist of an abnormal communication of arteries and veins without intervening capillaries that arises during development in prenatal period or just after birth.
- It grows in size with time and varies in size from several millimeters to several centimeters.
- The larger ones create a significant atrioventricular (AV) shunt (steal phenomenon) and considerable damage if they rupture.
- Supratentorial (90%).

PRESENTATION

- Small unruptured malformations present with headache or seizures.
- Larger malformations may present with progressive neurologic deficit.
- Hemorrhage is most often presentation (subarachnoid or intraparenchymal).

DIAGNOSIS

- Angiography is the test of choice and is required to direct the future therapy. MRA is also available.
- MRI or CT with contrast can demonstrate an AVM but provide less information than angiography.
- Photon knife is the treatment.

COMMON AVM VARIANTS

Vein of Galen Malformations

- Normal vein of Galen does not develop from its primitive vein, which persists and communicates with superior saggital sinus.
- Typically present during infancy with high-output congestive heart failure (CHF), failure to thrive, or enlarging head size.
- Mortality is 50%.

- Treatment in difficult embolization is preferred over surgery.
- A cranial bruit is often present with vein of Galen malformations.

Cavernous Hemangiomas

- Low-flow AVM with tendency to leak (cause seizure) but usually do not result in massive intracerebral hemorrhage.
- Retinal cavernous hemangiomas may be also present.
- Surgical resection is indicated if symptomatic.

Venous Angiomas

- Rarely symptomatic (seizures are the most common presenting sign).
- Surgery is not indicated unless complications arise.

TREATMENT

- Treatment consists of surgical resection or embolization.
- Focused gamma knife radiation has some benefits in smaller lesions.

Stroke

- Transient ischemic attacks (TIAs): Neurologic deficits that resolve in <24 hours.
- Stroke: Neurological deficits persist beyond 24 hours.

EPIDEMIOLOGY

- 2.6–13 cases per 100,000 per year.
- Hemorrhagic stroke 1.5–5 per 100,000 children per year.
- Ischemic stroke 0.6–8 per 100,000 children per year.

SIGNS AND SYMPTOMS

- Sudden onset of neurologic deficit or seizures in neonates.
- Headache, neck pain, and visual symptoms.

ETIOLOGY

- Pediatric causes of stroke differ from those in the adult population.
- Types of stroke include:
    - Ischemic: Thrombosis (both arterial and venous) or embolic (arterial).
    - Hemorrhage.
- A variety of conditions or risk factors exist for stroke, including:
    - AVMs.
    - Antiphospholipid antibodies/lupus anticoagulant.
    - Congenital coagulopathies such as factor V Leiden and deficiencies of protein C, S, and antithrombin III.
    - Hemoglobinopathies, sickle cell disease (SCD).
    - Sickle cell anemia at risk for ischemic stroke (sickling RBCs may → thrombosis or endothelial injury).
    - Cardiac conditions: Arrhythmias, myxoma, paradoxical emboli through a patent foramen ovale, and septic emboli from bacterial endocarditis.
    - Blunt trauma to the head and neck → arterial dissection.
    - Vasculitis, such as Kawasaki, hemolytic-uremic syndrome, systemic lupus erythematosus (SLE), meningitis.
    - Mitochondrial diseases.
    - Extracorporeal membrane oxygenation (ECMO) is a risk for both intracranial hemorrhage and embolic ischemic stroke.

EXAM TIP

Cardiac abnormalities are the most common cause of thromboembolic stroke in children.

CLINICALLY RELEVANT TYPES OF STROKE

Arterial Thrombosis/Embolism

- Intracerebral arterial dissection after trivial trauma to head and neck due to a tear in the intima.
- The cerebral area supplied by the vessel distal to lesion undergoes infarction and produces symptoms (loss of functions).
- Cerebral symptoms such as a progressive hemiplegia, lethargy, or aphasia result from the shedding of small emboli into the carotid circulation.
- Seizures are the most common presenting symptom in neonates.
- Cardiac source usually.

Venous Thrombosis

- May be subdivided into septic and nonseptic causes.
- Septic causes include bacterial meningitis, otitis media, and mastoiditis.
- Aseptic causes are numerous and include severe dehydration, hypercoagulable states, congenital heart disease, and hemoglobinopathies (SCD).
- Neonates present with diffuse neurologic signs and seizures.
- In children, focal neurologic signs are more common.

Closed Head Trauma

See Table 17-10 for a comparison of subdural and epidural hematomas.

> **EXAM TIP**
>
> Low-molecular-weight heparin has been shown to be safe, effective, and well tolerated in children with strokes.

SUBDURAL HEMATOMA (SDH)

EPIDEMIOLOGY

The most frequent focal brain injury in sports and the most common form of sports-related intracranial hemorrhage. Seen most often in infants, with a peak at 6 months.

TABLE 17-10. Features of Acute Epidural and Subdural Hematomas

Clinically it is not easy to differentiate the two, so head imaging helps differentiate between the two.

SUBDURAL HEMATOMA	EPIDURAL HEMATOMA
Follows inner layer of dura	Follows outer layer of dura (periosteum)
"Rounds the bend" to follow to follow falx or tentorium	Crosses falx or tentorium
Not affected by sutures of skull	Limited by sutures of skull (typically)
Tendency for crescentic shapes	Tendency for lentiform shapes
More mass effect than expected for their size	
Typical source of SDH: cortical vein	Typical source of EDH: skull fracture with arterial or sinus laceration

ETIOLOGY

- Occurs when a bridging vein is torn between the dura and the brain.
- In neonates due to a tear in tentorium near its junction with the falx.
- Trauma is usually the cause. Skull fracture is not seen commonly.
- An SDH should be ruled out if changes in conscious level are present after head injury.
- Typically frontoparietal location. It can be acute, subacute, or chronic.

SIGNS AND SYMPTOMS

- These depend on age of the child and also severity of the SDH.
- Neonates: Seizures, a bulging fontanelle, and ↓ activity.
- Retinal and preretinal hemorrhages common in children, especially in abused children.
- ↑ ICP (irritability, lethargy, vomiting, papilledema, headache).

DIAGNOSIS

Gold standard is CT scan.

EPIDURAL HEMATOMA

EPIDEMIOLOGY

Seen most often in children >2 years of age.

ETIOLOGY

- Most commonly results from a fracture in the temporal bone, lacerating the middle meningeal artery.
- Can be acute (arterial bleed) or chronic (venous bleed).
- Skull fracture is seen commonly.
- Nearly always unilateral; however, bilateral case has been described.

SIGNS AND SYMPTOMS

- Classic progression involves an initial loss of consciousness, followed by a lucid interval, and then abrupt deterioration and death (not as helpful in younger children).
- Hemorrhage and acute brain swelling cause ↑ ICP that can result in herniation with ispilateral ptosis, dilated pupil, and ipsilateral hemiparesis due to contralateral compression of crus cerebri.
- Retinal and preretinal hemorrhages are not common.
- ↑ ICP is seen (irritability, lethargy, vomiting, papilledema, headache).

DIAGNOSIS

Gold standard is CT scan.

TREATMENT

Epidural hematomas may progress rapidly, and immediate neurosurgical treatment is indicated.

COUP/CONTRECOUP INJURIES

Cerebral contusion injury mainly occurs when the head is subjected to a sudden acceleration or deceleration.

WARD TIP

Subdural hematomas appear crescent shaped (concave) on CT and will not cross the midline, but will cross ipsilateral suture lines.

WARD TIP

Lucid interval. *Think: Epidural hematoma.*

WARD TIP

Epidural hematomas appear lens shaped (convex) on CT and will not cross the midline or other cranial sutures.

EXAM TIP

Old contusions develop an orange color secondary to hemosiderin deposition and are referred to as *plaques jaunes* by pathologists.

Coup Injuries

- Located directly at the point of impact.
- More common in acceleration injuries such as being hit with a baseball bat.
- Multiple microhemorrhages as blood leaks into the brain tissue.

Contrecoup Injuries

- Located opposite (180 degrees) from the point of impact.
- More common in deceleration injuries, such as striking one's head on the pavement after a fall.

DIFFUSE AXONAL INJURY

EPIDEMIOLOGY

- Tissues with differing elastic properties shear against each other, tearing axons.
- Caused by rapid deceleration/rotation of head.
- Locations:
  - Cerebral hemispheres near gray-white junction.
  - Basal ganglia.
  - Corpus callosum, especially splenium.
  - Dorsal brain stem.
- High morbidity and mortality—common cause of posttraumatic vegetative state.
- Initial CT often normal despite poor GCS.
- Lesions often nonhemorrhagic and seen only on MRI.
- Survivors often have substantial long-term cognitive and behavioral morbidity.

Concussion

A teenage girl experienced a head-to-head collision with another player during soccer 4 hours ago. She reports headache, dizziness, nausea, and difficulty concentrating and focusing since the injury. She has no focal neurologic findings on examination. *Think: Concussion.*

- Trauma-induced brain dysfunction without demonstrable structural injury on standard neuroimaging.
- The signs and symptoms are nonspecific and may include:
  - Headache.
  - Fatigue.
  - Dizziness.
  - Nausea/vomiting.
  - Unsteadiness.
  - Mental fogginess.
  - Anterograde or retrograde amnesia.
  - Difficulties with concentration.
  - Sleep disturbances.
  - Emotional lability.
- Neuroimaging is normal in concussions and should only be used judiciously to rule out other pathology such as intracranial bleeds.

- The mainstay of management is physical and neurocognitive rest; however, low level of activity is not harmful.
- In addition, efforts to prevent additional injury though return to play guidelines that limit sports until full recovery is evident.
- Most pediatric patients will recover fully from concussions but caution is advised with repeat concussions.

Hydrocephalus

Head circumference >2 SD above the mean is macrocephaly, and if due to ↑ CSF in the CSF spaces, it is called hydrocephalus.

PHYSIOLOGY

- CSF is made by the choroid plexus in the walls of the lateral, third, and fourth ventricles.
- CSF flows in the following direction: lateral ventricles → foramen of Monro → third ventricle → cerebral aqueduct → fourth ventricle → foramina of Magendie and Luschka → subarachnoid space of spinal cord and brain → arachnoid villi.
- CSF is absorbed primarily by the arachnoid villi through tight junctions.

ETIOLOGY

- **Obstructive (noncommunicating) hydrocephalus:**
    - Most commonly due to stenosis or narrowing of the aqueduct of Sylvius.
    - An obstruction in the fourth ventricle is a common cause in children, including posterior fossa brain tumors, Arnold-Chiari malformations (type II), and Dandy-Walker syndrome.
    - Also seen in brain abscess, hematoma, infectious, vein of Galen malformation.
- **Nonobstructive (communicating) hydrocephalus:**
    - Most commonly follows a subarachnoid hemorrhage or meningitis.
    - Blood in the subarachnoid spaces may obliterate the cisterns or arachnoid villi and obstruct CSF flow.
    - Venous sinus thrombosis, meningeal malignancy, and intrauterine infections are other causes.
- **Ex vacuo:** Hydrocephalus resulting from ↓ brain parenchyma.

CLINICAL MANIFESTATIONS

- **Infants:**
    - Accelerated rate of enlargement of the head is most prominent sign.
    - Bulging anterior fontanelle (fontanelles can provide some pressure relief in infants, delaying symptoms of ↑ ICP). Widening of cranial sutures, sun-setting sign, and Parinaud syndrome.
    - Upper motor neuron signs such as brisk reflexes are common findings due to stretching of the descending cortical spinal tract.
    - ↑ ICP signs (lethargy, vomiting, headache, etc.) may be present, especially acutely.
- **Children and adolescents:**
    - Signs are more subtle because the cranial sutures are partially closed.
    - ↑ ICP signs may be present. Visual fields particularly peripheral fields are involved gradually. Papilledema can be present.
    - A gradual change in school performance may be the first clue to a slowly obstructing lesion.

EXAM TIP

The PECARN head trauma prediction rules have been shown to be accurate in the identification of children at very low risk for clinically important traumatic brain injuries and has resulted in decreased head CT utilization in children.

EXAM TIP

Pneumococcal and tuberculous meningitis produce a thick exudate that can obstruct the basal cisterns, → communicating hydrocephalus.

DIAGNOSIS

- A detailed history and physical exam is key to discovering the underlying etiology.
- Ultrasound and head CT/MRI are the most important studies to identify the cause of hydrocephalus.
- Familial cases of aqueductal stenosis have been reported and have an X-linked pattern of inheritance.
- Neurofibromatosis and meningitis have also been linked to aqueductal stenosis.

TREATMENT

- Medical management with acetazolamide (may ↓ CSF production) and furosemide may provide temporary relief.
- Placement of an extraventricular drain (EVD) or ventriculoperitoneal shunt (VPS), if the etiology is permanent, may be required.

Neoplasms

PEDIATRIC BRAIN TUMORS

EPIDEMIOLOGY

- Most common solid tumors of the childhood.
- Third most common pediatric tumors (#1 leukemia, #2 lymphoma).
- Supratentorial tumors are as common as infratentorial tumors.
- Glial cell tumors are the most common tumors in childhood and consist of astrocytomas, ependymomas, oligodendrioglioma, and primitive neuro-ectodermal tumor (PNET).
- Medulloblastoma is a common PNET only in childhood.

CLINICAL MANIFESTATIONS

- Generally present with either signs and symptoms of ↑ ICP (infants) or with focal neurologic signs (adolescents).
- Alterations in personality are often the first symptoms of a brain tumor.
- Nystagmus is the classic finding in posterior fossa tumors.
- Clinical signs depending on location of the tumor (loss/alteration in the functions of the brain area).
- Tumors in the posterior fossa tend to result in hydrocephalus secondary to CSF flow obstruction.

Cerebellar Astrocytoma

- The most common posterior fossa tumor of childhood.
- It is a slow-growing pilocytic astrocytoma and more benign than the adult-onset astrocytomas.
- Histologically shows fibrillary astrocytes with dense cytoplasmic inclusions called Rosenthal fibers.
- Associated with neurofibromatosis type 2 (NF2).
- Good prognosis; 5-year survival >90% after gross total resection which is achieved in 70% of the cases.
- Treatment is surgical resection.

Medulloblastoma (PNET)

- The second most common posterior fossa tumor and the most prevalent brain tumor in children under the age of 7 years. More common in males.

- Rapidly growing malignant tumor, arises from the undifferentiated neural cells in the region of cerebellar vermis.
- Tends to invade the fourth ventricle and spread along CSF pathways and involves the spine, so consider imaging the spine.
- Histologic analysis shows deeply staining nuclei with scant cytoplasm arranged in pseudorosettes.
- Presents with intracranial hypertension and ataxia, symptoms evolving in few weeks; papilledema is absent.
- MRI: Brightly enhancing mass with cystic lesion.
- **Treatment:** Surgical resection followed by irradiation.
- **Prognosis:** Dependent on size and dissemination of the tumor, 5-year survival rate is >80%.

Craniopharyngioma

- One of the most common supratentorial brain tumors of childhood which arises from cells in the Rathke's pouch.
- It is locally aggressive and recurs.
- Short stature or other endocrine-associated problems are common initial signs.
- Typically slow growing and benign.
- The tumor may be confined to the sella turcica or extend through the diaphragma sellae and compress the optic nerve or, rarely, obstruct CSF flow.
- Due to location, surgical resection is often subtotal.

DIAGNOSIS

- Ninety percent of craniopharyngiomas show calcification on CT scan; MRI provides better images of surrounding structures.
- Baseline endocrine studies and visual fields should be done prior to surgery.

Neuroblastoma (NB)

EPIDEMIOLOGY

- A common tumor of neural crest origin, representing the most common neoplasm in infants and 8% of all childhood malignancies.
- Malignant tumor that arises from the neural crest cells.
- Ninety percent are diagnosed before age 5, with a peak at 2 years.

PATHOGENESIS

NB is a small, round blue cell tumor with varying degrees of neuronal differentiation.

CLINICAL PRESENTATION

- The tumor may arise at any site of sympathetic nervous tissue.
- The adrenals, retroperitoneal sympathetic ganglia, and abdomen are the most common sites.
- Thirty percent arise in the cervical or thoracic region and may present with Horner syndrome.
- Opsoclonus-myoclonus: "Dancing eyes, dancing feet"—the telltale symptom of this disease (secondary to paraneoplastic antibodies).

DIAGNOSIS

- Typically, a mass is seen on CT or MRI.
- Ninety-five percent of cases have elevated tumor markers, most often homovanillic acid (HVA) and vanillylmandelic acid (VMA) in the urine.

WARD TIP

MRI is the best test for a posterior fossa tumor.

EXAM TIP

Infants tend to have localized NB in the cervical or thoracic region, whereas older children tend to have disseminated abdominal disease.

- Metaiodobenzylguanidine (MIBG) radioisotope scan for detecting small primaries and metastases.
- Stage 4: Infantile form, self-limited with good prognosis.
- Unfavorable prognosis is associated with ↑ neuron-specific enolase and amplification of N-*Myc* gene.
- Treatment is surgical resection followed by radio + chemotherapy.

Congenital Malformations

AGENESIS OF THE CORPUS CALLOSUM

- Associated with numerous syndromes and several inborn errors of metabolism, including patients with lissencephaly, Dandy-Walker syndrome, Arnold-Chiari type 2 malformations, and Aicardi syndrome.
- Imaging techniques reveal that the lateral ventricles are shifted laterally.
- Normal intelligence is not unusual, and often only mild clinical signs are seen.
- The severity of the disease varies greatly, from only mild deficits to marked retardation and severe epilepsy.

SYRINGOMYELIA

A teenage girl has a headache and a cape-like distribution of pain and temperature sensory loss that developed after a minor motor vehicle accident. *Think: Cervical syringomyelia with undiagnosed Chiari I.*

The Chiari type I malformation is characterized by herniation of the cerebellar tonsils through the foramen magnum and may → the development of syringomyelia. Common presentations include headache, neck pain, vertigo, sensory changes, and ataxia. Typical scenario is occipital pain precipitated by cough or Valsalva maneuver. MRI is the modality of choice.

- A slowly progressive paracentral cavity formation within the brain or spinal cord, most often in the cervical or lumbar regions.
- Thought to arise from incomplete closure of the neural tube during the fourth week of gestation.
- MRI is the test of choice for diagnosis.
- Often develops post-traumatically in the setting of an undiagnosed Chiari I malformation or tethered cord.
- Symptoms include bilateral impaired pain and temperature sensation due to decussation of these fibers near the central canal. Also weakness of the hand muscles and progressive symptoms as the cavity enlarges. It contains a yellow fluid.
- Called *syringobulbia* when present in brain stem.

DANDY-WALKER MALFORMATION

- Results from a developmental failure of the roof of the fourth ventricle to form, resulting in a cystic expansion into the posterior fossa.
- Ninety percent of patients have hydrocephalus.
- Agenesis of the cerebellar vermis and corpus callosum is also common.
- Infants present with a rapid ↑ in head size.
- Management is via shunting of the cystic cavity to prevent hydrocephalus.
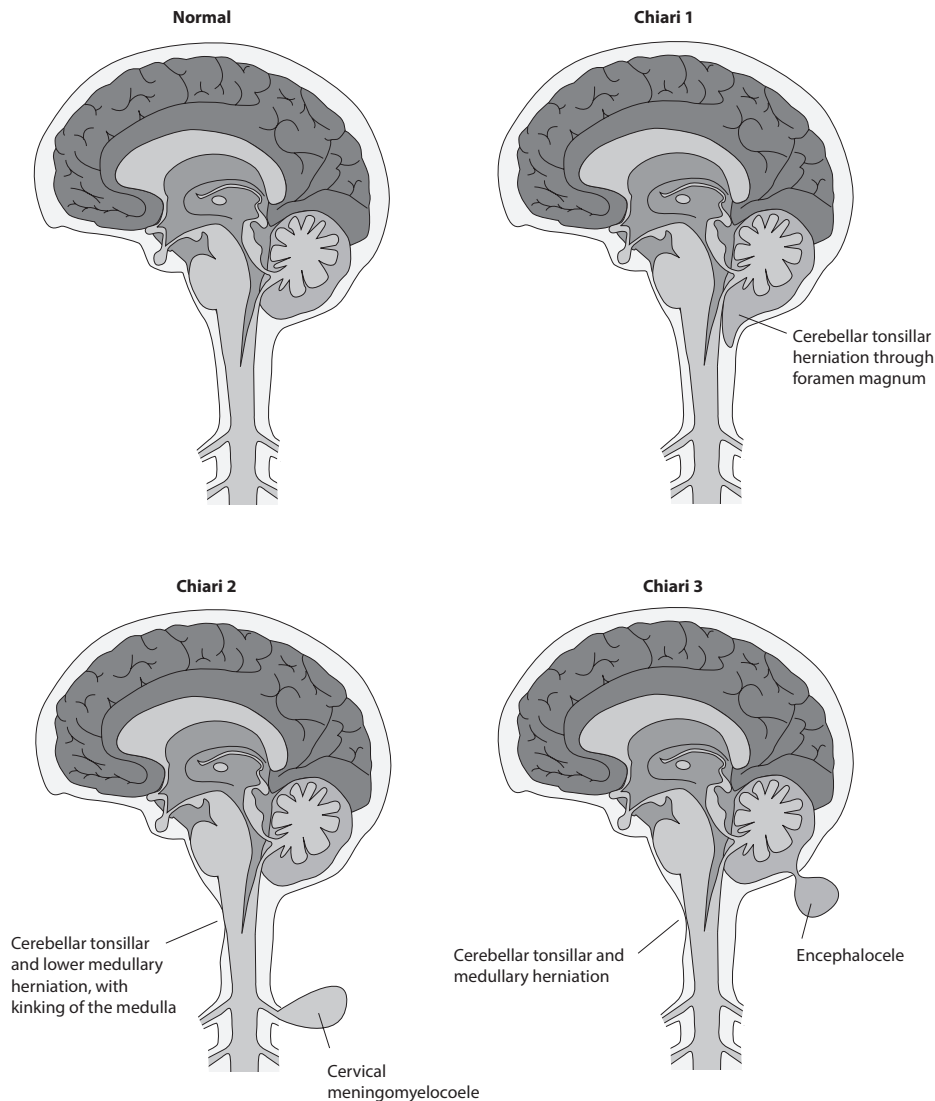
F I G U R E 1 7 - 7 . **The Chiari malformations.** Schematic representations of the Chiari malformations. Commonly associated hydrocephalus and syringomyelia not depicted.

ARNOLD-CHIARI MALFORMATIONS

- Four variations exist (see Figure 17-7), with type 2 being the most common, in which the cerebellum and medulla are shifted caudally, resulting in crowding of the upper spinal column.
- Type 2 is also associated with meningomyelocele in >95% of cases.
- Syringomyelia is associated in 70% of type 1, and 20–50% overall.
- Management includes close observation with serial MRIs and surgery as required.

Cerebral Palsy (CP)

DEFINITION

- A **non-progressive** disorder of movement and posture resulting from damage to the developing brain prior to or surrounding birth. If progressive, consider another diagnosis.
- Most cases occur in the absence of identifiable causes.

ETIOLOGY

- Prematurity with intraventricular hemorrhage.
- Birth or other asphyxia.
- Intrauterine growth retardation (IUGR), placental insufficiency.
- Infection: Prenatal/postnatal.
- Twin pregnancy.
- Chromosomal and genetic disorders.
- Head trauma.

SIGNS AND SYMPTOMS

- Prenatal and perinatal history.
- Delayed motor, language, or social skills.
- Not losing skills previously acquired.
- Feeding difficulties.
- Late-onset dystonia (ages 7–10 years).

EXAMINATION

- Hypertonia.
- Hyperreflexia.
- Posture and movement: May be spastic, ataxic, choreoathetoid, and dystonic.
- Abnormal primitive reflexes.
- Abnormal gait.
- Impaired growth of affected extremity.

ASSOCIATED PROBLEMS

- Seizure disorder.
- Mental retardation.
- Developmental disorders.

CLASSIFICATION

- Hemiplegic cerebral palsy: Upper limb involvement > lower limb; many walk before 2 years.
- Diplegic cerebral palsy.
- Quadriplegic cerebral palsy: Majority does not walk.
- Dystonic/athetoid cerebral palsy.
- Ataxic cerebral palsy.
- Monoplegic cerebral palsy: Usually lower limb and appears late.

TREATMENT

- Multidisciplinary approach with goals of maximizing function and minimizing impairment.
- Team includes general pediatrician, physiotherapist, occupational therapist, language therapist, neurologist, and social and educational support services.
- Orthopedic interventions are sometimes helpful.

Mental Retardation (MR)

DEFINITION

- Below average intellectual functioning in association with deficits in adaptive behavior prior to 18 years of age.
- Intelligence quotient (IQ) or developmental quotient (DQ) <70 or <2 standard deviations (SDs).

EPIDEMIOLOGY

- Affects 1–3% of the population.
- Approximately 75% are mild cases.
- Males are affected more than females.

SIGNS AND SYMPTOMS

- Significant delay in reaching developmental milestones.
- Delayed speech and language skills in toddlers with less severe MR.
- The child will continue to learn new skills depending on severity of MR.

DIAGNOSIS

Classification is based on IQ:
- Mild: IQ 55–70, 85% of cases.
- Moderate: IQ 40–55, 10% of cases.
- Severe: IQ 25–40, 3–5% of cases.
- Profound: IQ < 25, 1–2% of cases.

> **EXAM TIP**
>
> The IQ is scaled such that the mean is 100 and the standard deviation (SD) is 15. So MR is simply defined as an IQ two SDs below the mean.

Learning Disability (LD)

- Significant discrepancy between a person's intellectual ability and academic achievement.
- Often learn best in unconventional ways.
- Often restricted to a particular realm such as reading or mathematics with correspondingly discrepant scores on standardized measures of intelligence or academic achievement.
- Significant improvement with appropriate interventions.

NOTES

Special Organs—Eye, Ear, Nose

Eye

AMBLYOPIA

DEFINITION

A ↓ in visual acuity in one or both eyes caused by blurred retinal images leading to failure of the visual cortex to develop properly.

ETIOLOGY

- Strabismus.
- Refractive errors.
- Opacity in the visual path (e.g., cataract, ptosis, eyelid hemangioma).

DIAGNOSIS

Diagnosis is made by visual acuity testing.

TREATMENT

- Treatment of the pathology, such as removal of a cataract.
- Prescription glasses to correct refractive errors.
- Patching the good eye until the ambylopic eye has improved its vision.

STRABISMUS

DEFINITION

- Deviation or misalignment of the eye (see Figure 18-1).
- "To squint or to look obliquely."
- Strabismus can lead to vision loss which often results in permanent amblyopia.

DIAGNOSIS

- **Corneal light reflex:** The child looks directly into a light source and the doctor observes where the reflex lies in both eyes; if the light is off center in one pupil or asymmetric, then strabismus exists.
- **Alternative cover test:** The child stares at an object in the distance and the doctor covers one of the child's eyes; if there is movement of the uncovered eye once the other eye is covered, then strabismus exists.

TREATMENT

- Prescription glasses may help if the strabismus is secondary to refraction error.
- Extraocular muscle surgery may be necessary.
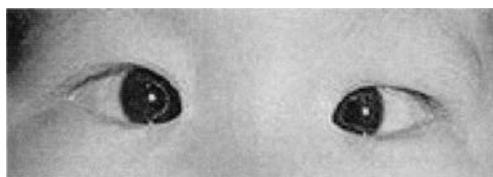
FIGURE 18-1. Child with strabismus.

OPTIC NEURITIS

DEFINITION

- Inflammation of the optic nerve.
- **Retrobulbar optic neuritis**: Without ophthalmoscopically visible signs of disc inflammation.
- **Papillitis or intraocular optic neuritis:** Ophthalmoscopically visible evidence of inflammation of the **nerve head.**
- Neuroretinitis: Inflammation of both the **retina and papilla.**

ETIOLOGY

- Idiopathic.
- Secondary to underlying disease—multiple sclerosis, lupus.
- Recent immunization or viral infection (measles, chickenpox, influenza).
- Extension from an infection involving the teeth, sinuses, or meninges.
- Side effect of treatment with vincristine or chloramphenicol.
- Secondary to a toxin such as lead.

SIGNS AND SYMPTOMS

- Loss of visio or central scotoma.
- Pain with extraocular motion.
- Pain to palpation of the globe.
- Afferent papillary defect.
- Bilateral in children (unilateral in adults).

COMPLICATIONS

- Color deficits.
- Motion perception deficits.
- Brightness sense deficits.

TREATMENT

A trial of intravenous (IV) steroids may ↓ the length of time for symptoms but has no effect on the outcome. Methylprednisolone also prolongs the onset to develop MS in those who are predisposed.

CONJUNCTIVITIS

DEFINITION

Inflammation of the conjunctiva.

TYPES

Allergic
- Immunoglobulin E (IgE)–mediated reaction caused by triggers such as pollen or dust.
- **Signs and symptoms:** Watery, itchy, red eyes with edema to the conjunctiva and lids. Typically bilateral.
- Pruritus and chemosis are common.
- **Treatment:** Includes removal of the trigger, cold compresses, and antihistamines.

EXAM TIP

A deviated eye is described as being turned "eso" (inward), "exo" (outward), "hypo" (downward), or "hyper" (upward) -tropic.

EXAM TIP

In children, optic neuritis is rarely associated with multiple sclerosis.

WARD TIP

Adenovirus is the most common viral cause of conjunctivitis.

Viral

- Adenovirus and coxsackievirus are typical causes.
- Adenovirus: Pharyngoconjunctival fever—triad: Pharyngitis, fever, and conjunctivitis.
- Epidemic keratoconjunctivitis: Fulminant vision-threatening condition with the involvement of cornea.
- **Signs and symptoms:** Watery, red eyes with preauricular lymph nodes.
- **Treatment:** Includes supportive treatment with constant hand washing to prevent transmission.

Bacterial

- Three organisms: Nontypeable *Haemophilus influenzae*, *Streptococcus pneumoniae*, and *Staphylococcus aureus.*
- Highly contagious, outbreaks can occur.
- **Signs and symptoms:** Mucopurulent discharge, red eyes, and edema of the conjunctiva. More often unilateral; can be bilateral.
- **Treatment:** Topical antibiotics (drops or ointment).

EPISCLERITIS/SCLERITIS

DEFINITION

Inflammation of the episclera or sclera.

ETIOLOGY

High association with autoimmune diseases.

SIGNS AND SYMPTOMS

- Eye pain.
- Photophobia.
- Erythema.
- ↓ visual acuity.
- Perforation is associated only with scleritis.

TREATMENT

- Topical steroids.
- Nonsteroidal anti-inflammatory drugs (NSAIDs).
- Immunosuppressive drugs in cases of steroid failure.
- Surgery for thinning or perforated sclera.

BLEPHARITIS

DEFINITION

Inflammation of the eyelid margins.

ETIOLOGY

- *Staphylococcus aureus.*
- *Staphylococcus epidermidis.*
- Seborrheic.
- A combination of the above.

SIGNS AND SYMPTOMS

- Burning.
- Itching.
- Erythema.

- Scaling.
- Ulceration of the lid margin.

TREATMENT

- Daily eyelid cleansing to remove scales.
- Topical antibiotics.

DACRYOSTENOSIS

A 4-month-old child presents with an exudative eye discharge and a painful, red lacrimal sac. *Think: Dacrocystitis.*

Dacrocystitis is the most common infection of the lacrimal system. It is often a complication of dacryocystocele. Excessive tearing, purulent eye discharge, and fever are the common symptoms. *S. aureus* and streptococci are the common organisms. Most patients require admission for intravenous antibiotics. An incision and drainage may be needed in the presence of a lacrimal sac abscess.

DEFINITION

A congenital nasolacrimal duct obstruction.

EPIDEMIOLOGY

Occurs in 5% of infants; appears a few weeks after birth.

ETIOLOGY

Failure of the epithelial cells of tear duct to come apart.

SIGNS AND SYMPTOMS

- Chronic tearing.
- Crusty discharge noted especially in AM. Typically without conjunctival injection.

COMPLICATIONS

Dacrocystitis—inflammation of the nasolacrimal sac; this must be treated with topical or systemic antibiotic and warm compresses.

TREATMENT

- Digital massage of the lacrimal sac and warm compresses are recommended, though it is unclear if they change the outcome from the natural course.
- Eyelid cleansing.
- Vast majority resolve before 1 year of age.
- Probing/instrumentation if still present after 1 year of age to rupture the membrane.

CHALAZION

DEFINITION

Inflammation of a meibomian (tarsal) gland leading to the formation of a granuloma.

SIGNS AND SYMPTOMS

- Firm nodule on the eyelid.
- Nontender.

> **EXAM TIP**
>
> Dacryostenosis is the most common disorder of the lacrimal system.

> **WARD TIP**
>
> Most dacryostenosis will resolve by 8 months of age.

TREATMENT

- Warm compresses.
- Excision if necessary.
- Most subside spontaneously over months.

HORDEOLUM

TYPES

- **External hordeolum,** or stye, is an infection of the glands of Zeis or Moll.
- **Internal hordeolum** is infection of the meibomian gland.

ETIOLOGY

S. aureus.

SIGNS AND SYMPTOMS

- Localized swelling.
- Tenderness.
- Erythema.

TREATMENT

- Warm compresses.
- Topical antibiotics general ineffective.
- Incision and drainage if there is no spontaneous rupture.

PERIORBITAL CELLULITIS

DEFINITION

Inflammation of the eyelids and periorbital tissue anterior to the septum.

ETIOLOGY

Extension of local infections including upper respiratory infection (URI), sinusitis, dental infection, facial cellulitis, trauma, or eyelid infection.

SIGNS AND SYMPTOMS

- Erythema.
- Edema.
- Induration and tenderness.
- No pain with extraocular movements.

COMPLICATIONS

Development of orbital cellulitis.

TREATMENT

Oral or IV antibiotics (e.g., ceftriaxone).

ORBITAL CELLULITIS

DEFINITION

Inflammation of the orbital tissues behind the septum.

ETIOLOGY

- Extension of a local infection including paranasal sinusitis, facial cellulitis, or dental abscess.
- Trauma.

WARD TIP

Orbital cellulitis is postseptal.

WARD TIP

Periorbital cellulitis is much more common than orbital cellulitis.

WARD TIP

The most common organisms causing both preorbital and orbital cellulitis—SHIP

S. aureus
H. influenzae
S. Pneumoniae

- The most common organisms are *H. influenza, S. aureus,* and *S. pneumoniae.*
- Most common site: Medial orbital wall.
- ↑ incidence secondary to ↑ in methicillin-resistant *S. aureus* (MRSA).
- Orbital cellulitis is caused most commonly by ethmoid sinusitis.

SIGNS AND SYMPTOMS

- Proptosis, ophthalmoplegia, and ↓ vision differentiate it from preseptal cellulitis.
- Painful extraocular motion is often the first sign.
- Proptosis is classic, but late, sign.
- Decreased visual acuity.
- Erythema in conjunctiva.
- Edema.

DIAGNOSIS

Orbital computed tomography (CT) scan with IV contrast.

TREATMENT

- **Ophthalmology consultation.**
- Intravenous antibiotics, possible surgical drainage.

COMPLICATIONS

- Loss of vision.
- Meningitis.
- Central nervous system (epidural) abscess.

> **WARD TIP**
>
> Periorbital cellulitis is preseptal.

CORNEAL ULCER

ETIOLOGY

- Trauma (sand, contact lens, etc.) with secondary infection. Often preceded by a traumatic corneal abrasion.
- Bacterial: *Pseudomonas aeruginosa, Neisseria gonorrhoeae.*
- Fungal: Especially in contact lens users.

SIGNS AND SYMPTOMS

- Corneal haze.
- Painful.
- Photophobia.
- Tearing.

COMPLICATIONS

- Perforation.
- Scarring.
- Blindness.

> **EXAM TIP**
>
> Retinoblastoma gene: Mutation in the long arm of chromosome 13.

DIAGNOSIS

- Slit-lamp exam: Fluorescein staining reveals an epithelial defect.
- Scraping of the cornea to identify infectious etiology.

TREATMENT

- Local antibiotics.
- In some cases, systemic treatment may be required.

> **WARD TIP**
>
> **Must** evaluate for the presence of retinoblastoma in a child presenting with strabismus.

RETINOBLASTOMA

- The most common primary ocular malignancy in children.
- Average age: 18 months (90% <5 years).

SIGNS AND SYMPTOMS

- Leukocoria: White pupillary reflex is the most common presentation.
- Strabismus is the second most common presentation.
- Orbital inflammation.
- Hyphema: Blood layering anterior to the iris.
- May be bilateral (40%).

DIAGNOSIS

- Direct visualization during eye exam.
- Computed tomography (CT) or ultrasound (US) can help confirm and evaluate spread.

TREATMENT

- Chemotherapy.
- Laser photocoagulation.
- Cryotherapy.
- Enucleation for unresponsive tumors.
- Referral for genetic counseling for families with a history of retinoblastoma.

Ear

OTITIS MEDIA

DEFINITION

Inflammation of the middle ear.

EPIDEMIOLOGY

- The incidence of otitis media is higher in:
    - Boys.
    - Children in day care.
    - Children exposed to secondhand smoke.
    - Non-breast-fed infants.
    - Immunocompromised children,
    - Children with craniofacial defects like cleft palate,
    - Children with a strong family history for otitis media,
- The incidence of infection is higher in children because of their eustachian tube anatomy:
    - Horizontal.
    - Short in length.
    - ↓ tone.

ETIOLOGY

- *S. pneumoniae.*
- *H. influenzae.*
- *Moraxella catarrhalis.*

COMPLICATIONS

- Hearing loss due to persistent middle-ear effusion.
- Perforation.

EXAM TIP

Retinoblastoma is the most common primary malignant intraocular tumor in children.

WARD TIP

Family members of a patient with retinoblastoma should be checked because it may be hereditary.

EXAM TIP

The most common overall complication of otitis media is hearing loss.

- Mastoiditis.
- Cholesteatoma: Saclike epithelial structures.
- Facial nerve paralysis: The facial nerve may not be completely covered with bone in the middle ear; therefore, infection can spread to the nerve.
- Labyrinthitis.
- Abscess formation.
- Tympanosclerosis: Scarring of the tympanic membrane.
- Meningitis.

ACUTE OTITIS MEDIA

Eustachian tube dysfunction is the most important factor.

SIGNS AND SYMPTOMS

- Ear tugging.
- Ear pain.
- Fever.
- Malaise.
- Irritability.
- Hearing loss.
- Nausea and vomiting.

DIAGNOSIS

- Diagnosis is made with a pneumatic otoscope—the tympanic membrane will have ↓ mobility and will appear hyperemic and bulging with loss of landmarks.
- Tympanocentesis should be used as an adjunct in patients who are <8 weeks old, are immunocompromised, have a complication, or were treated with multiple courses of antibiotics without improvement; the fluid is sent for culture and sensitivity.

TREATMENT

- Typically, the first-line antibiotic is amoxicillin. High dose can be used for cases most likely to be resistant (antibiotics within 3 months, less than 2 years of age, in day care or with sibling in school or day care).
- Antipyretics: Ibuprofen and/or acetaminophen.
- Topical anesthetic eardrops (e.g., benzocaine).
- For healthy children >2 years old with milder case, watchful waiting for 24–48 hours is an option.
- Pneumococcal vaccine has reduced the incidence of acute otitis media.

RECURRENT ACUTE OTITIS MEDIA

DEFINITION

Three to four episodes of acute otitis media in 6 months or 6 episodes in a year.

TREATMENT

- Prophylactic antibiotics.
- Myringotomy and ventilating tubes should be considered.

OTITIS MEDIA WITH EFFUSION

SIGNS AND SYMPTOMS

- Hearing loss.
- Dizziness.

EXAM TIP

The most common intracranial complication of otitis media is meningitis.

WARD TIP

Remember that younger children who are unable to communicate may have only nonspecific signs like nausea and vomiting with an acute illness such as acute otitis media.

WARD TIP

A red eardrum in a crying child is normal; the most specific sign of acute otitis media is ↓ mobility of the tympanic membrane.

- *No* fever.
- *No* ear pain.

DIAGNOSIS

Pneumatic otoscope shows a retracted eardrum with loss of landmarks and air-fluid levels or bubbles.

TREATMENT

- If asymptomatic, a child is observed for 3 months to see if effusion resolves.
- If symptomatic after 3 months of observation, treatment includes antibiotics and possibly myringotomy and insertion of tympanostomy tubes.

OTITIS EXTERNA

A 4-year-old boy presents with what looks like herpetic vesicles in the ear canal and tympanic membrane. *Think: Ramsay Hunt syndrome* (facial paralysis + herpes zoster oticus). CN VIII involved = sensorineural hearing loss or vertigo.

It is due to herpetic involvement of the facial (geniculate), vestibulocochlear, or trigeminal ganglia which results in pain and vesicular eruptions about the auricle and external ear canal.

DEFINITION

- Inflammation of the external auditory canal.
- Occurs when trauma introduces bacteria into an area that is excessively wet or dry.

ETIOLOGY

- Bacterial: *P. aeruginosa, S. aureus, Proteus mirabilis, Klebsiella pneumoniae.*
- Viral: HSV/Zoster.
- Fungal: *Candida.*

SIGNS AND SYMPTOMS

- Ear pain with movement of the tragus or pinna.
- Pruritus of the ear canal.
- Edema of the ear canal.
- Otorrhea: Usually white in color.
- Palpable lymph nodes: Peri- and preauricular.
- Normal tympanic membrane.

COMPLICATIONS

- Malignant otitis externa leads to hearing loss, vertigo, and facial nerve paralysis.
- Temporary hearing loss secondary to swelling.
- Necrotizing otitis externa:
  - *Pseudomonas* osteomyelitis in the temporal bone.
  - Risk factors: Diabetes, immunocompromised (*Aspergillus fumigatus*).

DIAGNOSIS

Diagnosis is made by otoscopic examination.

TREATMENT

Topical antibiotics and steroids to reduce edema (e.g., Cortisporin suspension [hydrocortisone-polymyxin-neomycin-bacitracin]).

WARD TIP

Otitis externa is known as "swimmer's ear."

EXAM TIP

Malignant otitis externa is caused by *P. aeruginosa* and must be treated systemically (i.e., oral or IV antibiotics; NOT drops alone).

MASTOIDITIS

DEFINITION

- Inflammation of the mastoid air cells in the temporal bone.
- Most common pathogen: S. *pneumoniae*.

Acute Mastoiditis

- Mostly seen in children after/with an acute otitis media.
- If resolution does not occur, may lead to acute mastoiditis with periosteitis, acute mastoid osteitis, or chronic mastoiditis.
- Fever.
- Pain and induration behind the ear overlying mastoid air cells and temporal bone.
- Erythema and tenderness over the mastoid area.

Acute Mastoiditis with Periosteitis

- Includes the involvement of the periosteum.
- **Treatment:** Includes myringotomy with ventilation tube placement and IV antibiotics.

Acute Mastoid Osteitis

- Occurs when there is an empyema and destruction of the mastoid cells.
- The child will have a tender, swollen, red mastoid process with the ear displaced down and out.
- **Treatment:** Includes IV antibiotics, and mastoidectomy may be necessary.

Chronic Mastoiditis

Involves treatment with antibiotics and possibly a mastoidectomy if osteitis is present.

COMPLICATIONS

- Hearing loss.
- Facial nerve palsy.
- Subperiosteal abscess.
- Cranial osteomyelitis.
- Labyrinthitis.
- Intracranial spread (meningitis, epidural or cerebellar abscess, subdural empyema).
- Dural sinus thrombosis.

TINNITUS

DEFINITION

- Ringing in the ear.
- Commonly found in children who have middle-ear disease or hearing loss. Also associated with salicylate use.

VERTIGO

DEFINITION

Dizziness with the feeling that one's body is in motion.

T A B L E   1 8 - 1 .   **Ototoxic Drugs**

Diuretics	**Furosemide**
	Ethacrynic acid
Antibiotics	**Aminoglycosides**
	Minocycline
	Quinolones
Chemotherapeutics	Cisplatin
	Vinblastine
Antimalarials	Quinine
	Chloroquine
	Mefloquine
Antiarrhythmics	Quinidine
Salicylates	Aspirin

SIGNS AND SYMPTOMS

- Difficulty walking straight, or stumbling.
- Spinning sensation.
- Vomiting.

ETIOLOGY

May occur secondary to the following conditions:
- Otitis media.
- Labyrinthitis.
- Trauma.
- Cholesteatoma.
- BPV.
- Ménière disease.
- CNS disease.

TREATMENT

Address the underlying cause.

OTOTOXIC DRUGS

See Table 18-1.

Nose

SINUSITIS

DEFINITION

Inflammation of the membranes covering the sinuses. Clinical definition also includes minimum duration of 10 days of symptoms that are worsening.

Sinus Development

- Ethmoid sinus at birth.
- Maxillary sinus at birth.
- Sphenoid sinus 5 years.
- Frontal sinus 7 years.

Etiology

- A child may be at risk for sinusitis if there is an obstruction or cilia impairment.
- S. *pneumoniae*.
- H. *influenzae*.
- M. *catarrhalis*.
- Rhinovirus is the most common viral pathogen.
- Bacterial sinusitis is usually preceded by a viral upper respiratory infection.

Predispositions

- Occlusion of the sinus ostium.
- Cystic fibrosis.
- Allergy/asthma.
- Cyanotic congenital heart disease.
- Dental infections.

Signs and Symptoms

- Headache—worse when bending foward.
- Sinus tenderness to palpation.
- Persistent nasal discharge (purulent) >10 days' duration.
- Halitosis.
- Cough secondary to postnasal drip.
- Early AM nausea or emesis.

Complications

- Cellulitis.
- Abscess formation.
- Osteomyelitis.
- Meningitis may occur through spread of the ethmoid, sphenoid, or frontal sinuses.

Diagnosis

- Diagnosis is made clinically.
- If imaging is required, a CT scan is preferred over plain films, which are not as sensitive.

Treatment

- First line is amoxicillin for 14–21 days.
- If no improvement, a macrolide or amoxicillin-clavulanate may be used.
- Decongestants.
- Nasal saline drops/mist.
- Nasal irrigation.

EPISTAXIS

Definition

- Nosebleed.
- Common age: 2–10 years.
- Unusual during infancy; must consider coagulopathy or nasal organic causes (e.g., choanal atresia).

> **EXAM TIP**
>
> At birth, only the maxillary and ethmoid sinuses are present.

> **WARD TIP**
>
> The most common location for epistaxis in children is from the anterior nasal septum because Kiesselbach's plexus is located there.

> **WARD TIP**
>
> Blood in vomit may be present if a child has swallowed blood from epistaxis; always ask about epistaxis if a patient presents with hematemesis.

ETIOLOGY

- The most common location for a nosebleed in children is the anterior septum.
- The most common cause is trauma secondary to a fingernail.
- Other causes may include foreign bodies, inflammation, or dry air.
- If a child has recurrent, severe epistaxis, more serious causes should be looked into such as thrombocytopenia, clotting deficiencies, and angiofibromas.

SIGNS AND SYMPTOMS

Bleeding may occur from one or both nostrils.

TREATMENT

- Compression for 10 minutes with head tilted forward.
- Cold compresses to the nose.
- Topical vasoconstrictors may allow visualization and identification of the bleeding site.
- Cauterization using silver nitrite.
- Packing the nose.

ALLERGIC RHINITIS

DEFINITION

An IgE-mediated response to an allergen causing an inflammation of the nasal mucous membranes.

SIGNS AND SYMPTOMS

- Generally does not develop until 2–3 years of age.
- Sneezing.
- Watery nasal discharge.
- Red, watery eyes.
- Itchy ears, eyes, nose, and throat.
- Nasal obstruction secondary to edema.

DIAGNOSIS

Characteristic findings on physical exam:
- Boggy, bluish mucous membranes of the nose.
- Dark circles under the lower eyelids ("allergic shiners").
- Allergic salute (transverse nasal crease from rubbing and pushing the nose up with your hand).
- A smear of nasal secretions will show a high number of eosinophils.

TREATMENT

- Avoid triggers.
- Antihistamines.
- Decongestants.
- Cromolyn nasal solution.
- Topical steroids.

CHOANAL ATRESIA

DEFINITION

- A separation of the nose and pharynx by a membrane or bone (90%); may be unilateral or bilateral.
- The most common congenital anomaly of the nose.

SIGNS AND SYMPTOMS

- Each child's presentation will differ depending on his or her ability to mouth breathe.
- Respiratory distress that improves as the child cries because the mouth is open.
- Cyanosis, especially when the child is feeding or sucking. Crying relieves the cyanosis.

DIAGNOSIS

- Inability to pass a catheter through one or both nostrils.
- CT will show the extent of the atresia.

TREATMENT

- Prompt placement of an oral airway, maintaining the mouth in an open position or intubation.
- Maintaining an open airway by an orogastric tube or large nipple.
- Tracheostomy or intubation may be required depending on the severity.
- The ultimate treatment is surgical correction.

WARD TIP

Restenosis of corrected choanal atresia is common.

NOTES

Musculoskeletal Disease

Normal Skeletal Maturation

- The growth plate in the newborn is generally not constituted as an effective structure until 12–24 months.
- Many plain radiographs are mostly lucent due to the cartilaginous composition of developing skeletal structure.
- The metaphysis is the most metabolically active area.

Pediatric Skeleton

- The anatomy, biomechanics, and physiology of the child's skeleton are very different when compared to adults, → differences in fracture pattern, diagnostic problems, and treatment regimens.
- Bone is more porous and elastic than in adults or older adolescents.
- The most obvious anatomic differences in the pediatric bones are the presence of growth plates (physes) and the thick periosteum.
- The physis (growth plate) is the weakest site in a child's bone.
- A thick periosteal sleeve makes fractures more stable.
- These features make fractures along the physis more common than sprains (opposite to the injury pattern after skeletal maturation).

Osteomyelitis

A previously ambulatory 18-month-old girl refuses to walk. She has marked tenderness over the distal left femur. The child has a temperature of 101.6°F (38.7°C), erythrocyte sedimentation rate (ESR) of 72 mm/hr, and white blood cell (WBC) count of 18.5. Radiographs reveal no bony abnormalities. *Think: Osteomyelitis.*

The initial signs and symptoms are often nonspecific. Refusal to walk, limping, or reluctance to move the affected extremity is common presentation. Fever is usually present. Focal tenderness over a long bone may be an important clue for diagnosis. The WBC count is usually ↑ and ESR is elevated. Initial plain radiograph may be normal or show only soft tissue swelling. Radionuclide bone scans usually are positive within 48–72 hours of onset of illness. However, MRI has mostly replaced nuclear medicine studies as the imaging modality of choice for osteomyelitis. Bone aspiration may reveal an etiologic agent.

DEFINITION

- Inflammation of the bone caused by infection.
- Can be acute (<2 weeks) or chronic.

EPIDEMIOLOGY

- Preschool-age children (50%).
- Male preponderance.
- More common in African-American children.

ETIOLOGY

- Most often bacterial.
- See Table 19-1 for causes of osteomyelitis by age group.
- Overall, *Staphylococcus aureus* is the most common bug.

TABLE 19-1.   Causes of Osteomyelitis by Age

AGE GROUP	ORGANISMS
Infants <1 year, especially under age 3 months	*Staphylococcus aureus* *Streptococcus agalactiae* *Escherichia coli*
<5 years	*S. aureus* *Streptococcus pyogenes* *Streptococcus pneumoniae* *Kingella kingae*
>5 years	*S. aureus* *S. pyogenes*
Adolescent	*Neisseria gonorrhoeae*

PATHOPHYSIOLOGY

- Primarily hematogenous.
- Spread from contiguous infected structures.
- Direct inoculation.
- Occult injury without breaking skin may also lead to susceptibility to osteomyelitis in that area (thought to disrupt normal blood flow and make bacterial adherence more likely).

SIGNS AND SYMPTOMS

- Infants and young children:
    - Fever, irritability, and lethargy.
    - Refusal to walk or bear weight.
- Older children:
    - May localize pain.
    - Limping.
- Physical examination:
    - Painful local swelling.
    - Point tenderness.
    - Local warmth.
    - Erythema.

DIAGNOSIS

- Leukocytosis.
- Elevated ESR: Sensitive marker for osteomyelitis, mean ~70 mm/hr. Peaks 3–5 days.
- Elevated C-reactive protein (CRP): Peaks at 48 hours.
- CRP typically returns to normal 7–10 days after appropriate therapy but the ESR may remain elevated for 3 or 4 weeks, even with appropriate therapy.
- Growth on blood culture.
- Radiographic findings (see Figure 19-1):
    - Lucent areas in bone represent cortical destruction.
    - Periosteal elevation. Periosteal and lytic changes in the bone may not be seen until substantial bone destruction has occurred.
    - Plain films are typically normal for up to 14 days in up to two-thirds of children.

WARD TIP

The most common site for osteomyelitis is the rapidly growing end (metaphysis) of long bones.

EXAM TIP

Nearly 50% of hematogenous osteomyelitis occurs in the tibia or femur.

WARD TIP

Consider osteomyelitis in any child with ↓ use of a limb and fever.

FIGURE 19-1. **Acute hematogenous osteomyelitis of the proximal humerus.** Mottling and patchy radiolucencies are present in the metaphyseal region. (Reproduced, with permission, from Wilson FC, Lin PP. *General Orthopedics.* New York: McGraw-Hill, 1997.)

- Magnetic resonance imaging (MRI):
    - Provides anatomic detail not seen with bone scan.
    - Useful for visualizing soft tissue abscess associated with osteomyelitis, bone marrow edema, and bone destruction.
    - Contrast enhancement with gadolinium.
    - Has become imaging modality of choice due to high sensitivity *and* specificity.
- Radionuclide scintigraphy (bone scan):
    - Common isotopes used include technetium, gallium, and indium.
    - Can detect osteomyelitis within 24–48 hours of onset with ~90% sensitivity.
    - *Caution:* Radionuclide scans may be positive in other illnesses that result in ↑ osteoblastic activity, including malignancy, trauma, cellulitis, postsurgery, and arthritis (poor specificity).

DIFFERENTIAL DIAGNOSIS

- Septic arthritis (can coexist).
- Fracture.
- Cellulitis.
- Transient synovitis.
- Acute leukemia or neuroblastoma.
- Slipped capital femoral epiphysis (SCFE).
- Soft tissue injury or infection.

TREATMENT

- Admit all children with osteomyelitis.
- Orthopedic consultation.

- Parenteral antibiotics pending cultures (obtain blood, bone, and joint aspirate cultures before antibiotic administration when possible).
- Infants and children: Penicillinase-resistant penicillin (oxacillin) and cephalosporin (cefotaxime).
- Older children (>5 years): Nafcillin or vancomycin.
- Consider surgical drainage if:
  - There is clear abscess on imaging.
  - Pus is obtained from aspirate.
  - No response to 24–48 hours of antibiotics.

COMPLICATIONS

- Pathologic fractures.
- Chronic osteomyelitis.
- Leg length discrepancy.

Septic Arthritis

> A 14-year-old boy presents to the emergency department (ED) because of right knee pain for the past 2 days. Three days prior to the onset of the pain, he hit his knee on a pool table. Vitals: Temperature 100.6°F (38.1°C), pulse rate 100, respirations 24. On physical exam, the knee is swollen and tender and is held in flexion. This patient has a high suspicion for septic arthritis. *Think: The most important initial diagnostic procedure is aspiration of the knee for smear and culture.*
>
> Although more common in children, it occurs in all ages. Trauma can be the precipitant of infection. *Staphylococcus aureus* is the most common cause of septic arthritis. Physical examination may show local erythema, warmth, and swelling. The key to the diagnosis is the detection of bacteria in the synovial fluid either by Gram stain or by a culture; therefore, synovial fluid aspiration should be performed.

> A 5-year-old boy who has a definite history of penicillin allergy develops osteomyelitis. Smear of the aspirate shows gram-positive cocci in clusters. *Think: Treat child with vancomycin.*
>
> Vancomycin is directed against gram-positive organisms and can be given to patients who cannot receive penicillins and cephalosporins and is the initial antibiotic of choice if one suspects MRSA.

DEFINITION

A microbial invasion of joint space.

ETIOLOGY

- Neonates:
  - *S. aureus* (most common cause of septic arthritis in all ages).
  - *S. agalactiae.*
  - Gram-negative enteric bacilli (*K. kingae* has replaced *Haemophilus influenzae* type b [Hib] as the most common gram-negative arthritis in the child 2 months to 5 years old).
- Older children (very similar to osteomyelitis):
  - *S. aureus:* Remember that infection with community-acquired methicillin-resistant *S. aureus* (CA-MRSA) is becoming more common.
  - *S. pyogenes.*
  - *S. pneumoniae.*
  - Gonococcus.

WARD TIP

Osteomyelitis without radiographic change should not be treated with antibiotics until an osseous specimen is obtained.

EXAM TIP

Most common cause of polyarticular septic arthritis is *Neisseria gonorrhoeae.*

WARD TIP

Adolescent intravenous (IV) drug abusers are at risk for gram-negative septic arthritis.

WARD TIP

Candida albicans must also be considered in neonates and premature infants with septic arthritis.

EPIDEMIOLOGY

Relatively common in infancy and childhood; can occur in all ages.

PATHOPHYSIOLOGY

Organisms may invade the joint by:
- Direct inoculation.
- Contiguous spread.
- Hematogenous (most common route).

SIGNS AND SYMPTOMS

- Pain with passive range of motion.
- Joint stiffness.
- Erythema.
- Edema.
- Limp and unable to bear weight.

LABORATORY

- Complete blood count (CBC)—a normal WBC does not rule out diagnosis.
- Elevated ESR.
- Blood culture.
- Joint aspiration.

MANAGEMENT

- Admit all children with septic arthritis.
- Orthopedic consultation (it is an orthopedic emergency) and often intra-operative washout of joint.
- Joint aspiration.
- Parenteral antibiotics immediately after joint aspiration.

COMPLICATIONS

Potential for severe complications:
- Spread—results in osteomyelitis.
- Avascular necrosis.
- Angular deformities.
- Leg length discrepancy.

Transient Synovitis

An 18-month-old infant presents with a limp that progressed to refusal to bear weight on her left leg. When lying in bed she is not in any distress but has pain with range of motion of left hip. There is no swelling, redness, warmth noted. Patient recently recovered from febrile URI but has had no fever for 4 days.

DEFINITION

- A reactive arthritis.
- The most common cause of hip pain in childhood.
- Predominates in children 2–5 years old but happens up to 10 years of age.

ETIOLOGY

- Cause remains uncertain.
- Often follows an upper respiratory infection (URI).

Signs and Symptoms

- Unilateral hip or groin pain is the most common complaint.
- Painful limp.
- Usually afebrile and nontoxic appearance.

Diagnosis

- Diagnosis of exclusion. Transient synovitis must be distinguished from septic arthritis. The two disorders may have a similar presentation. Where doubt exists, ultrasound-guided or fluoroscopically guided diagnostic aspiration should be performed.
- Radiographs are usually normal.
- Plain films do not diagnose or exclude a hip effusion.
- The appearance of a septic arthritis of the hip may be identical.
- Most patients will have fluid in the joint visible on ultrasound which does not distinguish septic arthritis from transient synovitis.

Management

- First, rule out septic arthritis.
- Supportive therapy.
- Nonsteroidal anti-inflammatory drugs (NSAIDs).
- Complete recovery occurs within a few weeks.

Osgood-Schlatter Disease

A 16-year-old boy complains of right knee pain. He is active in multiple sports. On examination, there is significant tenderness and swelling over the tibial tuberosity. He is otherwise healthy. *Think: Osgood-Schlatter disease;* treat with activity restriction.

Osgood-Schlatter disease is a chronic overuse injury and a common cause of knee pain. It occurs due to forceful contraction of the extensor mechanism in sports such as jumping. It is a clinical diagnosis. Tenderness over the proximal tibial tuberosity at the site of patellar insertion is often present. However, plain radiographs are helpful to rule out other causes of knee pain.

Definition

- An inflammatory disorder of the proximal tibial physis where the patellar tendon inserts on the tibia.
- Benign, self-limited extra-articular disease.

Etiology

- Traction apophysitis/repetitive trauma.
- Chronic microtrauma to the tibial tuberosity secondary to overuse of the quadriceps muscle.

Risk Factors

- Boys between ages 11 and 18 years.
- Rapid skeletal growth.
- Involvement in repetitive jumping sports.

Signs and Symptoms

- Knee pain (tibial tuberosity pain).
- Reproduced by extending the knee against resistance.
- Knee joint examination is normal.
- Tibial tuberosity swelling.
- Absence of effusion or condylar tenderness.

WARD TIP

Pain is most pronounced over the tibial tubercle in Osgood-Schlatter disease.

WARD TIP

Typical history: Nonspecific aching knee pain exacerbated by exercise.

WARD TIP

Osgood-Schlatter disease is a common cause of knee pain in the adolescent.

WARD TIP

Septic arthritis may coexist with osteomyelitis at sites where the metaphysis lies *within* the joint capsule:

- Proximal femur–hip joint
- Proximal humerus–shoulder joint
- Distal lateral tibia–ankle joint
- Proximal radius–elbow joint

F I G U R E   1 9 - 2 . **Osgood-Schlatter disease.** Note the elevation and irregularity of the tibial tubercle. (Reproduced, with permission, from Wilson FC, Lin PP. *General Orthopedics.* New York: McGraw-Hill, 1997.)

DIAGNOSIS

- Diagnosis is primarily clinical.
- X-ray of the knee may show evidence of fragmentation of the tibial tubercle (see Figure 19-2) or calcification on the patellar tendon. Compare with opposite side.

TREATMENT

- Relative rest.
- Restriction of activities as tolerated (patients can still engage in activities even with pain; they will eventually grow out of it).
- Knee immobilizer only for severe cases.
- Complete resolution through physeal closure.

Legg-Calvé-Perthes Disease

A 6-year-old boy presents with hip and knee pain. He has been limping. On examination, he is unable to abduct or internally rotate his hip. *Think: Legg-Calvé-Perthes disease.*

Legg-Calvé-Perthes disease is osteonecrosis of the capital femoral epiphysis of the femoral head. It is due to vascular changes within the proximal femur. Limping is the most common symptom. Pain may be poorly localized in the groin or referred to the thigh or knee joint. It is therefore important to recognize that thigh or knee pain in the child may be due to hip pathology. Plain x-rays of the hip are helpful in making the diagnosis. It occurs at an earlier age than slipped capital femoral epiphysis (SCFE).

DEFINITION

Avascular necrosis of femoral head (occurs when blood supply to the proximal femoral epiphysis is disrupted).

ETIOLOGY

- Idiopathic.
- Some precipitants include sickle cell disease, steroids, trauma, and infection.

EPIDEMIOLOGY

- Male-to-female ratio: 4:1.
- Highest incidence is during periods of rapid growth of the epiphyses (ages 4–8 years).

SIGNS AND SYMPTOMS

- Insidious onset. Symptoms generally begin with minor trauma.
- Limp with or without pain.
- Pain (activity related and relieved by rest).
- Limited hip motion, particularly abduction and medial rotation.
- ↓ range of motion.
- Knee pain is common.

RADIOLOGY

- Anteroposterior (AP) and frog-leg lateral position. X-ray findings correlate with the progression and extent of necrosis (see Figure 19-3).
- Early: Effusion of the joint, widening of the joint space and periarticular swelling.
- Initial radiographs are typically normal. Later in the course there is decreased bone density around the joint, collapse of the femoral head (affected side appears smaller than the unaffected femoral head).
- Late: New bone replaces necrotic bone.

MANAGEMENT

- Pediatric orthopedic consultation.
- Protect joint.
- Abduction orthoses to "contain" the femoral head on the acetabulum.
- Rest and NSAIDs.
- Surgery for 6- to 10-year-olds with large areas of necrosis.

COMPLICATIONS

Limb length discrepancy.

> **EXAM TIP**
>
> Toxic synovitis is the most common cause of limping and acute hip pain in children aged 3–10 years.

> **WARD TIP**
>
> Classic presentation of Legg-Calvé-Perthes disease is a "painless limp."
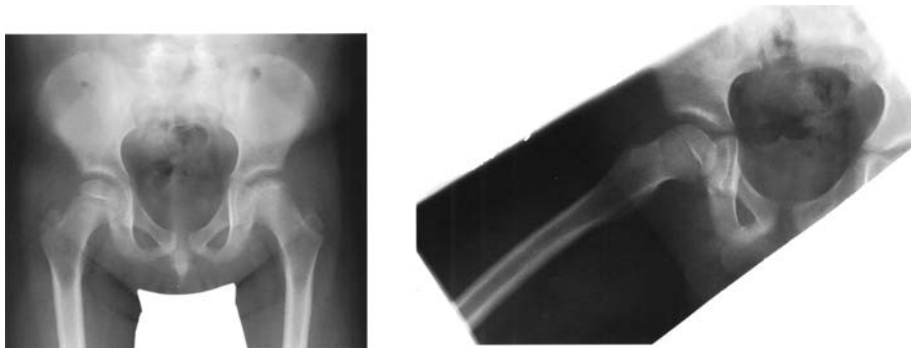
FIGURE 19-3. **Radiograph of pelvis demonstrating changes of Legg-Calvé-Perthes disease.** Note the sclerotic, flattened, and fragmented right femoral head.

Slipped Capital Femoral Epiphysis (SCFE)

An obese 14-year-old boy has pain in the left anterior thigh for 2 months. On physical exam, there is limited passive flexion and internal rotation of his hip. *Think: The most likely diagnosis is SCFE.*

SCFE is the most common hip disorder of adolescence and occurs at the time of the pubertal growth spurt. Referred pain (groin, thigh, or knee pain) is a common presentation. AP and frog-leg lateral views of the pelvis should be obtained.

DEFINITION
- Type of Salter I fracture of the proximal femoral growth plate.
- Disruption of the proximal femoral epiphysis through the physeal plate.
- Epiphysis is usually displaced medially and posteriorly.

ETIOLOGY
- Most cases are idiopathic.
- Weak growth plate (physis is weak prior to closure).
- Local trauma.

TYPES
Other than acute (<3 weeks) and chronic (>3 weeks) forms, between 20% and 40% of SCFEs are bilateral even if it is not evident on the x-ray.

RISK FACTORS
- Obesity.
- Hypothyroidism.
- Hypogonadism.
- Growth hormone (GH) administration.
- Renal osteodystrophy.
- Radiation therapy.

SIGNS AND SYMPTOMS
- Pain can be located anywhere between the groin and medial knee.
- Limping.
- Internal rotation, flexion, and abduction are lost.
- Painful limp.
- Leg tends to roll into external rotation.

DIAGNOSIS
- AP and frog-leg lateral of both hips (Figure 19-4).
  - Ice cream scoop (epiphysis) falling off its cone.
  - The frog-leg lateral film demonstrates subtle displacement more clearly.
- Earliest sign is widening of epiphysis.
- Always examine and obtain x-ray of the contralateral hip.
- A diagnosis of a preslip can be made with bone scintigraphy.
- MRI is sensitive for this condition.

COMPLICATIONS
- Avascular necrosis of capital femoral epiphysis.
- Chondrolysis.
- Nonunion.
- Premature closure of the epiphyseal plate.
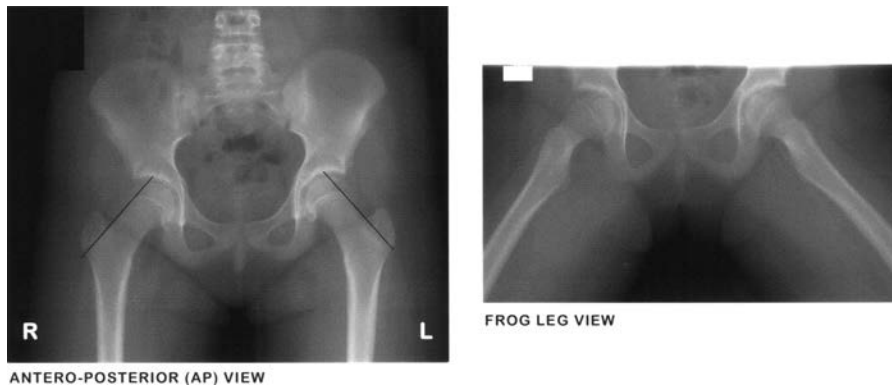
FIGURE 19-4. Hip radiographs in a 13-year-old girl with mildly slipped capital femoral epiphysis (SCFE) on the right. Note on the AP view that a line drawn along the superior border of the femoral neck (Klein line) shows less femoral head superior to the line on the right than it does in the normal hip on the left.

FIGURE 19-5. SCFE after screw fixation (same patient as Figure 19-4).

TREATMENT

- Orthopedic consultation.
- Removal of weight bearing from the affected limb (crutches or wheelchair in overweight patients).
- Internal fixation using central percutaneous pin fixation with one or more cannulated screws is the treatment of choice (Figure 19-5).

Tenosynovitis

DEFINITION

Inflammation of the tendon and tendon sheath.

ETIOLOGY

- Trauma—penetrating injury can cause infection of the tendon and tendon sheath which is a surgical emergency.
- Overuse.

> **EXAM TIP**
>
> Bilateral SCFE is common. It occurs in approximately 20% of cases.

TYPES

- de Quervain tenosynovitis of the wrist (i.e., abductor pollicis longus and extensor pollicis brevis tendons).
- Volar flexor tenosynovitis (i.e., trigger finger).

MANAGEMENT

- Rest.
- NSAIDs.
- Thumb spica wrist splint.
- Surgical drainage and irrigation is necessary in infectious circumstances to prevent contractures due to inflammation and scarring.

The Limping Child

- Thorough history and physical.
- Assess gait with patient barefoot based on age.
- Plain-film radiographs typically initial study.
- Consider lab work based on differential diagnosis (i.e., CBC, ESR).

DIFFERENTIAL DIAGNOSIS

AGE RANGE	DIFFERENTIAL DIAGNOSIS
0–4	Hip dysplasia Synovitis Toddler's fracture
4–10 years old	Toxic synovitis (also called transient synovitis) Juvenile idiopathic arthritis Legg-Calvé-Perthes
10–18 years old	SCFE Osgood-Schlatter Gonococcal arthritis Fracture
All ages	Sprain Contusion Osteomyelitis Septic arthritis Neoplasm

Juvenile Idiopathic Arthritis (JIA)

DEFINITION

Chronic disease characterized by inflammation of the joints.

ETIOLOGY

Unknown.

CLASSIFICATION

- **Polyarticular** (35%):
  - Five or more joints.
  - Symmetric distribution.
  - Both large and small joints.
- **Pauciarticular** (50%):
  - Fewer than five joints.
  - Asymmetric distribution.
  - Often large weight-bearing joints.
  - Iridocyclitis (50%).
- **Systemic** (20%):
  - Fever, rash, arthritis, and visceral involvement.
  - Also known as Still disease.

DIAGNOSTIC CRITERIA

- Age of onset under 16 years.
- Arthritis in one or more joints.
- Duration ≥6 weeks with history of remitting and recurring symptoms.
- Exclusion of other causes.
- See Table 19-2 for diagnosis based on joint fluid analysis.

SIGNS AND SYMPTOMS

- **Polyarticular:**
  - Symmetric, chronic pain and swelling of joints.
  - Systemic features are less prominent.
  - Long-term arthritis; symptoms wax and wane.
- **Pauciarticular:**
  - Asymmetric chronic arthritis of a few large joints.
  - Systemic features are uncommon.
- **Systemic:**
  - Salmon-pink macular rash.
  - Systemic symptoms: Arthritis, hepatosplenomegaly, leukocytosis, and polyserositis.
  - Episodic, remission of systemic features within 1 year.

TREATMENT

The goal of treatment is to restore function, relieve pain, and maintain joint motion.

- NSAIDs.
- Range-of-motion and muscle-strengthening exercises.
- Methotrexate, anti-tumor necrosis factor (TNF) antibodies, or antipyrimidine medication for patients who do not respond to NSAIDs.

> **EXAM TIP**
>
> The most common cause of chest pain in children is idiopathic.

> **WARD TIP**
>
> Rheumatoid factor (RF) tends to be negative in early childhood in JRA. In fact, it is so uncommon that the nomenclature has changed to JIA to reflect the rarity of RF positivity status in children.

> **WARD TIP**
>
> A normal ESR does not exclude the diagnosis of JRA.

TABLE 19-2. Joint Fluid Analysis

DISORDER	CELLS/ML	GLUCOSE
Trauma	RBC > WBC < 2000 WBC	Normal
Reactive arthritis	2000–10,000 mononuclear WBC	Normal
Juvenile rheumatoid arthritis	5000–50,000 WBC, mostly neutrophils	Low to normal
Septic arthritis	>50,000 WBC, usually >90% neutrophils	Low to normal

Reproduced, with permission, from Hay WW, et al. *Current Pediatric Diagnosis and Treatment,* 14th ed. New York: McGraw-Hill, 2002.

Reiter Syndrome

DEFINITION

Triad of asymmetric arthritis, urethritis, and uveitis.

ETIOLOGY

Thought to be a reactive arthritis after infection with gram-negative organisms (*Salmonella, Shigella, Yersinia, Campylobacter, Chlamydia, Mycoplasma,* and *Ureaplasma*) in persons with human lymphocyte antigen (HLA)-B27.

DIAGNOSIS

- Bone density is preserved.
- Proliferative bone formation is present.

Childhood Fractures (Not Related to Abuse)

TORUS FRACTURE (FIGURE 19-6)

- Latin *torus* = buckle.
- Buckle fracture: Occurs with axial loading onto long bone under compression (e.g.: FOOSH = fall on outstretched hand).

TORUS

FIGURE 19-6. Torus fracture.
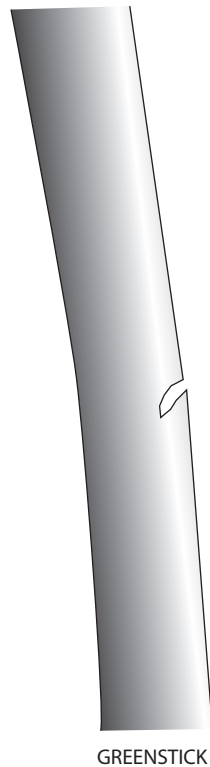
GREENSTICK

F I G U R E 1 9 - 7 .   Greenstick fracture.

- Impaction injury in children in which the bone cortex is buckled but not disrupted.
- Stable fracture.

GREENSTICK FRACTURE (FIGURE 19-7)

- **Definition:** A break in the convex cortex under tension caused by the bending of malleable bone.
- Incomplete fracture in which cortex is disrupted on only one side.
- Represents bone failure on the tension side and a plastic or bend deformity on the compression side.

TODDLER FRACTURE (FIGURE 19-8)

- Nondisplaced spiral fracture of the tibia.
- Symptoms include pain, refusal to walk, and minor swelling.
- There is often no history of trauma, or a history of a twisting motion of the leg with a planted foot. Can happen with seemingly very minor mechanism.
- **Treatment:** Immobilization for a few weeks to protect the limb and to relieve pain.

SALTER-HARRIS FRACTURE CLASSIFICATION

See Figure 19-9.

WARD TIP

Reiter syndrome: Can't pee, can't see, can't climb a tree.

WARD TIP

Spiral fractures are rarely non-accidental trauma (NAT). Bucket-handle fractures of the metaphaseal corner of long bones are thought to be pathognomonic for NAT.

FIGURE 19-8. **Toddler fracture.** (Reproduced, with permission, from Schwartz DT, Reisdorff BJ. *Emergency Radiology*. New York: McGraw-Hill, 2000: 602.)

Salter-Harris Type I:
• Fracture throught the physis (growth plate only)
• Often seen in children < 5 years
• Only visible radiographically if the physis is widened, distorted or the epiphysis is distorted

Salter-Haris Type II:
• Through the metaphysis and the physis
• Most common sites are distal radius & tibia

Salter-Harris Type III:
• Through the epiphysis and physis
• Most common sites are knee ankle

Salter-Harris Type IV:
• Through the epiphysis, physis, and metaphysis
• Most common site is lateral condyle of humerus
• Can produce joint defomity and chronic disability

Salter-Harris Type V:
• Crush injury of the physis
• May appear as a narrowing of the growth plate lucency
• Often not radiographically visible
• May lead to premature fusion
• The proximal tibia is the most common site for growth disturbance
• Mechanism is axial compression

FIGURE 19-9. **Salter-Harris fracture classification.**

Sprains

DEFINITION

- **Sprain:** Injury to ligament.
- **Strain:** Injury to muscle-tendon unit.

ANKLE SPRAIN

- **Inversion:** Injury to lateral ligament (85%).
  - Anterior talofibular injures first.
  - Posterior talofibular—severe pain.
- **Eversion:** Injury to medial ligament (15%).
  - Deltoid ligament injury most common.
  - More severe than inversion.

SIGNS AND SYMPTOMS

- Grade I: Pain/tenderness without loss of motion.
- Grade II: Pain/tenderness, ecchymosis with some loss of range of motion.
- Grade III: Ligament is completely disrupted; pain/tenderness, swelling and ecchymosis, joint instability, and complete loss of range of motion.

MANAGEMENT

- The goal of treatment is to ↓ local edema and residual stiffness.
- RICE therapy—rest, ice, compression, elevation.
- Protection includes joint immobilization at a right angle, elastic (Ace) bandage wrap, and Jones's dressing (a padded, bulky dressing with cotton curlex and elastic wrap) for more severe injuries. Splinting the affected joint protects against injury and relieves swelling and pain.
- Crutches and crutch gait training.
- NSAIDs as needed for analgesia.
- Early use of joint and appropriate rehabilitation is key to healing process.

Subluxation of Radial Head

A 2-year-old boy complains of left arm pain. He holds his arm in a flexed, pronated position and refuses to supinate his forearm during examination. His mother remembers pulling him by the arm yesterday. *Think: Subluxation of the radial head (nursemaid's elbow).*

Subluxation of the radial head is a common traumatic elbow injury in children. Average age is between 2 and 4 years. It is due to a sudden longitudinal pull on the forearm while the child's arm is in pronation. Child keeps his arm in passive pronation, with slight flexion at the elbow. Radiographs are not required if the history is suggestive of this injury.

DEFINITION

Subluxation of the radial head.

ETIOLOGY

- Slippage of the head of the radius under the annular ligament.
- Most common cause is axial traction (e.g., holding onto the hand when the child falls). It may happen with unencumbered fall as mechanism as well.
- Sudden longitudinal pull on the forearm while the child's arm is in pronation.
- Stretching of the annular ligament allows fibers to slip between the capitellum and the head of the radius.

EPIDEMIOLOGY

- Common age: 1–4 years.
- More frequent under 2 years.
- Rare after the age of 6 years (annular ligament becomes thick and strong by age 5 years).

SIGNS AND SYMPTOMS

- Child suddenly refuses to use an arm.
- Elbow fully pronated/inability of the child to supinate the arm.

DIAGNOSIS

- Diagnosis is made primarily by history.
- Imaging studies are unnecessary.
- No swelling or bony tenderness on exam.

MANAGEMENT

- Elbow is placed in full supination and slowly moved to full flexion.
- Alternatively, overpronation with full extension of the forearm is also effective.
- A click at the level of the radial head signifies reduction (see Figure 19-10).
- Relief of pain is remarkable and rapid.
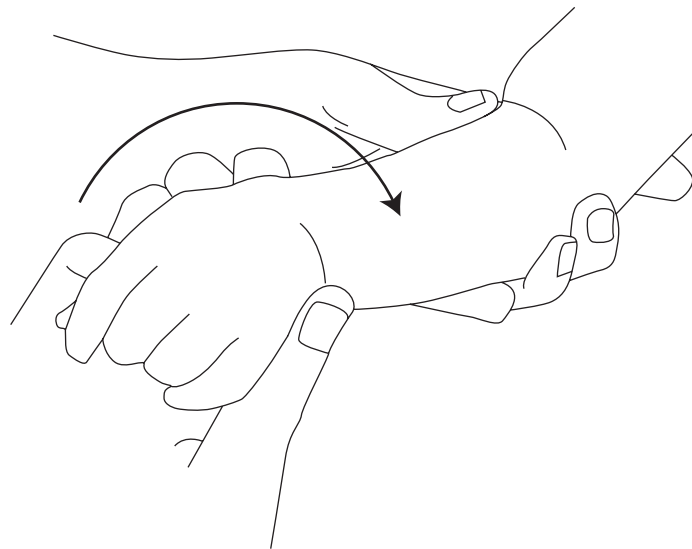
FIGURE 19-10. Reduction of nursemaid's elbow.

Osteosarcoma

👤 A patient has had dull, aching pain for several months that has suddenly become more severe. *Think: Osteosarcoma.*

Osteosarcoma is a common cancer in adolescence. Symptoms may be present for a significant period of time before it is diagnosed. Pain, particularly with activity, is a common symptom. Distal femur and proximal tibia are commonly involved bones. On examination, palpable mass may be present. Since osteosarcoma is not radiosensitive, surgery may be needed.

DEFINITION

Malignant tumor arising from osteoblasts.

EPIDEMIOLOGY

- The most frequent sites of origin are the metaphyseal regions.
- Most osteosarcomas develop in patients 10–20 years of age.
- Osteosarcomas most frequently occur during periods of maximal growth.

SIGNS AND SYMPTOMS

- Bone pain.
- Typically long bones (distal femur and proximal tibia) and flat bones (pelvis 10%).

RADIOLOGY

Radiographs show mixed sclerotic and lytic lesion arising in the metaphyseal region, often described as a *sunburst pattern* with periosteal elevation (Figure 19-11).

> **EXAM TIP**
>
> Osteosarcoma is the sixth most common malignancy in children and the third most common in adolescents.

> **EXAM TIP**
>
> Osteosarcoma is the most common primary malignant neoplasm of bone (60%).

> **WARD TIP**
>
> All patients with osteosarcoma should undergo computed tomographic (CT) scanning to detect metastatic pulmonary disease.

FIGURE 19-11. **Osteosarcoma of proximal humerus.** Note disorganized appearance of bony cortex (arrow).

MANAGEMENT

- Bone tumors generally are sensitive to radiation and chemotherapy.
- Amputation and limb salvage are effective in achieving local control.

PROGNOSIS

- Seventy-five percent survival in nonmetastatic disease.
- Death is usually due to pulmonary metastasis.
- Widely metastatic disease carries poor prognosis.

Ewing Sarcoma

A 10-year-old boy complains of pain in his left leg. On examination, there is localized swelling and pain in the middle of his left femur. His temperature is 100.8°F (38.2°C), and ESR is elevated. Further questioning reveals a 2-month history of increasing fatigue and weight loss. *Think: Ewing sarcoma.*

Ewing sarcoma is a common malignant bone tumor in young patients. Most patients present with either pain or a mass. Most common site for metastases is lung. Periosteal reaction and new bone formation with an onion-skin appearance are suggestive of Ewing sarcoma. Most tumors are considered radiosensitive.

DEFINITION

Malignant tumor of bone arising in medullary tissue.

EPIDEMIOLOGY

- Most common bone lesion in first decade.
- Second to osteosarcoma in second decade.
- However, still rare—only 200 new cases/yr.
- Very strong Caucasian and male predilection, hereditary.

SIGNS AND SYMPTOMS

- Bone pain.
- Systemic signs: Fever, weight loss, fatigue.

RADIOLOGY

- Calcified periosteal elevation, termed *onion skin*.
- Radiolucent lytic bone lesions in the diaphyseal region.
- Evaluation of patients with Ewing's sarcoma should include a CT to define the extent of metastatic disease.

TREATMENT

- Radiotherapy.
- Chemotherapy.
- Surgical resection.
- Autologous bone marrow transplant for high-risk patients.

PROGNOSIS

- Patients with a small localized tumor have a 50–70% long-term disease-free survival rate.
- Patients with metastatic disease have a poor prognosis.

> **EXAM TIP**
>
> Primary site is split almost evenly between the extremities and central axis.

> **EXAM TIP**
>
> Bone pain is a presenting symptom of Ewing sarcoma in 80–90%.

> **EXAM TIP**
>
> Metastasis is present in 25% of patients with Ewing's sarcoma at diagnosis. The most common sites of metastasis are the lungs, bone (spine), and bone marrow.

Benign Bone Tumors

OSTEOID OSTEOMA

DEFINITION

Reactive lesion of bone.

SIGNS AND SYMPTOMS

- Pain (evening or at night), relieved with aspirin.
- Point tenderness.
- Predominantly found in boys.

RADIOLOGY

Osteosclerosis surrounds small radiolucent nidus.

MANAGEMENT

- Salicylates relieve pain.
- Surgical incision of the nidus is curative.

PROGNOSIS

Prognosis is excellent. There have been no known cases of malignant transformation, although the lesion has been known to reoccur.

ENCHONDROMA

DEFINITION

Cartilaginous lesions.

SIGNS AND SYMPTOMS

- Tubular bones of hands and feet.
- Pathologic fractures.
- Swollen bone.
- Ollier disease (if multiple lesions are present).

RADIOLOGY

- Radiolucent diaphyseal or metaphyseal lesion.
- Often described as "fingernail streaks in bones."

MANAGEMENT

Surgical curettage and bone grafting.

PROGNOSIS

Prognosis is excellent. Malignant transformation may occur, but is very rare in childhood.

OSTEOCHONDROMA (EXOSTOSIS)

DEFINITION

- Most common bone tumor in children.
- Disturbance in enchondral growth.
- Benign cartilage-capped protrusion of osseous tissue arising from the surface of bone.

<div style="float:right;">

WARD TIP

Osteoid osteomas are most common in the femur and tibia.

EXAM TIP

Enchondromas have a predilection for the phalanges.

</div>

SIGNS AND SYMPTOMS

- Painless, hard, nontender mass.
- Distal metaphysis of femur, proximal humerus, and proximal tibia.
- Grows with child until skeletal maturity.

RADIOLOGY

Pedunculated or sessile mass in the metaphyseal region of long bones.

MANAGEMENT

Excision if symptomatic.

PROGNOSIS

Prognosis is excellent. Malignant transformation is very rare.

BAKER CYSTS

DEFINITION

- Herniation of the synovium in the knee joint into the popliteal region.
- A Baker cyst is lined by a true synovium, as it is an extension of the knee joint.

SIGNS AND SYMPTOMS

- Popliteal mass often with discomfort.
- Commonly transilluminates.

DIAGNOSIS

Aspiration of mucinous fluid from popliteal fossa.

MANAGEMENT

- Baker cysts are benign.
- Nearly always disappears with time in children.
- Avoid surgery (only for significant pain).

Developmental Dysplasia of the Hip (DDH)

While doing a physical exam on a 3-month-old female infant, the physician notices that her left knee is lower when her hips are flexed. The infant was born to a P1G1 mother via a breech vaginal delivery. *Think: DDH.*

It is called Galeazzi sign, which is an apparent shortening of the femur on the side of the dislocated hip and is noted by placing both hips in 90 degrees of flexion and comparing the height of the knees. Screening examination should include the Ortolani test and the provocative maneuver of Barlow. Risk factors include female gender, breech presentation, and positive family history for DDH. Ultrasound can be obtained in infants younger than 6 months. It is a treatable condition with successful treatment if intervention starts early. Pavlik harness is the treatment of choice in the first 6 months of life.

DEFINITION

Abnormal growth and development of the hip resulting in an abnormal relationship between the proximal femur and the acetabulum.

EPIDEMIOLOGY

- One in 1000 live births.
- Tenfold ↑ risk in sibling of child with DDH.
- Female > male. Breech female is at highest risk.

PATHOPHYSIOLOGY

- At birth there is a lack of development of both acetabulum and femur.
- Progressive with growth.
- Reversible if corrected in first few days or weeks.

SIGNS AND SYMPTOMS

- **Newborn:**
    - Ortolani: Reduction maneuver.
    - Barlow: Provocative test → potential for dislocation of a nondisplaced hip.
    - Asymmetric skin folds (40%).
- **3–6 months:**
    - Limited abduction.
    - Allis's or Galeazzi's sign: Knee is lower on affected side when hips are flexed.
- **12 months (unilateral dislocation):** Trendelenburg sign—painless limp and lurch to the affected side with ambulation. When the child stands on the affected leg, there is a dip of the pelvis on the opposite side, due to a weakness of the gluteus medius muscle.
- **12 months (bilateral dislocation):**
    - Waddling gait.
    - Lumbar lordosis due to flexion contractures.

IMAGING

- <6 months: Ultrasound (acetabulum and proximal femur are predominantly cartilaginous).
- >6 months: Radiographs (proximal femoral epiphysis ossifies by 4–6 months).

TREATMENT

- **Newborn to 6 months:** Pavlik harness (flexion and abduction of the hip). Must remain in place for several months for treatment to be effective.
- **6 months to 3 years:** Skin traction for 3 weeks to relax soft tissues around the hip prior to closed or open reduction. After 6 months of age, the failure rate for the Pavlik harness is >50%.
- **>3 years:** Operations to correct deformities of the acetabulum and femur.

Osteogenesis Imperfecta (OI)

A 2-year-old child is brought in with a right radial fracture after lightly bumping his arm. An x-ray shows multiple healing fractures. On examination, the child has blue sclera, thin skin, and hypoplastic teeth. *Think: OI.*

OI is also called brittle bone disease. Triad: Fragile bones, blue sclerae, and early deafness. The teeth frequently have dentinogenesis imperfecta. The enamel is normal, but the dentin is dysplastic. Radiographic appearance may vary according to the type of disease and its severity and include osteopenia and fractures. In infancy, these features may result in evaluation for nonaccidental injury.

WARD TIP

Barlow test: Dislocate the hip by flexing and adducting the hip with axial pressure.

WARD TIP

Forced abduction of the hips in DDH is contraindicated because of risk of avascular necrosis.

WARD TIP

Signs of instability are more reliable than x-ray in DDH.

EXAM TIP

In DDH, after 3–6 months, muscle contractures develop, and the Barlow and Ortolani tests become negative.

WARD TIP

Triple diapers have no place in the treatment of DDH.

WARD TIP

Double or triple diapers are not adequate to obtain a proper position and are no longer indicated treatment of DDH.

DEFINITION

- Rare, inherited disorder of connective tissue, characterized by poor bone mineralization leading to multiple and recurrent fractures.
- OI is an autosomal-dominant disorder that occurs in all racial and ethnic groups.

ETIOLOGY

- Molecular genetics have identified more than 150 mutations in the genes that encode for type 1 collagen.
- There are four types of OI: Types I and IV are mild and present with an ↑ risk of fractures. Type II is lethal in the newborn period, and type III is a severe form causing significant bony deformity secondary to multiple fractures.
- Ten percent of OI patients have the severe neonatal form of the disease.

SIGNS AND SYMPTOMS

- Bone fragility.
- Easy bruising.
- Repeated fracture after mild trauma.
- Deafness.
- Blue sclera.
- Hyperextensibility of ligaments.
- Normal intelligence.

DIAGNOSIS

Radiographic findings:
- Osteopenia.
- Wormian bones ("floating" intrasutural bones of the skull seen in OI).
- Thin cortices.
- Bowing.
- Normal callus formation.
- Collagen synthesis analysis.

TREATMENT

- Bisphosphonates.
- Surgical correction of long-bone deformities.
- Trauma prevention.

PROGNOSIS

Prognosis is poor, and most patients are confined to wheelchairs by adulthood.

GENETIC COUNSELING

- Genetic counseling should be offered.
- Risk of an affected individual passing the gene to his or her offspring is 50%.

Klippel-Feil Syndrome

DEFINITION

Congenital fusion of a variable number of cervical vertebrae.

ETIOLOGY

Failure of normal segmentation in the cervical spine.

SIGNS AND SYMPTOMS

- Classic clinical triad:
    - Short neck.
    - Low hairline.
    - Limitation of neck motion.
- Associated with:
    - Renal anomalies.
    - Scoliosis.
    - Spina bifida.
    - Deafness.

DIAGNOSIS

Children with Klippel-Feil syndrome should have the following tests performed:
- Renal ultrasound.
- Hearing test.
- Lateral flexion-extension radiographs of cervical spine under fluoroscopy.

TREATMENT

- Annual evaluation.
- Avoid high contact sports.
- Close evaluation of immediate family members.

Torticollis

DEFINITION

Twisted or wry neck.

ETIOLOGY

- **Congenital:** Injury to the sternocleidomastoid muscle during delivery.
- **Acquired:** Rotatory subluxation of the upper cervical spine.

MANAGEMENT

- **Congenital:** Physical therapy for stretching.
- **Acquired:**
    - Warm soaks.
    - Analgesics.
    - Mild anti-inflammatory agents.
    - Soft cervical collar.
    - Passive stretching.

> **EXAM TIP**
>
> Torqueo = to twist; collum = neck

> **EXAM TIP**
>
> Torticollis is the most common cause of neck muscle strain.

Muscular Dystrophies

DUCHENNE MUSCULAR DYSTROPHY (DMD)

A 3-year-old boy must use his hands to push himself up when rising from a seated position. *Think: Gower's maneuver.*

The Gower test indicates proximal muscle weakness, which is described as a ↓ in the ability to rise from the floor without assistance of the upper extremities. DMD is a sex-linked recessive inherited trait that occurs in males. Since children with DMD usually reach early motor milestones at appropriate times, diagnosis may be delayed. However, the diagnosis becomes evident between 3 and 6 years of age. Creatine kinase (CK) should be obtained, which is elevated (50–100 times normal). DNA analysis confirms the diagnosis.

DEFINITION

Degenerative disease of muscles. DMD is characterized by early childhood onset, typically within the first 5 years.

INHERITANCE

- X-linked recessive.
- One in 3600 males.

SIGNS AND SYMPTOMS

- Clumsiness.
- Easy fatigability.
- Symmetric involvement.
- Axial and proximal before distal.
- Pelvic girdle, with shoulder girdle usually later.
- Rapid progression.
- Loss of ambulation by 8–12 years.
- Pseudohypertrophy of calves.
- Cardiomegaly—varied severity.

DIAGNOSIS

- Serum CK is markedly elevated.
- Muscle biopsy is pathognomonic—degeneration and variation in fiber size and proliferation of connective tissue. No dystrophin present.

MANAGEMENT

- Encourage ambulation.
- Prevent contractures with passive stretching.

BECKER MUSCULAR DYSTROPHY (BMD)

DEFINITION

Milder form of muscular dystrophy.

INHERITANCE

X-linked recessive.

SIGNS AND SYMPTOMS

- Late childhood onset, typically between 5 and 15 years.
- Slow progression.
- Proximal muscle weakness.
- Prominence of calf muscles.
- Inability to walk occurs after 16 years.

DIAGNOSIS

Muscle biopsy shows degeneration of muscle fibers. Dystrophin is reduced or abnormal.

MYOTONIC MUSCULAR DYSTROPHY (MMD)

INHERITANCE

Autosomal dominant.

SIGNS AND SYMPTOMS

- Congenital MMD affects infants and is more severe than the adult form.
- Adult-onset MMD has a variable onset, typically in the teens to adulthood.
- Muscle weakness of voluntary muscles in the face, distal limbs, and diaphragm.
- Involuntary clenching of hands and jaw, ptosis, and respiratory difficulty.

LIMB GIRDLE MUSCULAR DYSTROPHY

DEFINITION

Two types:
- Pelvifemoral (Leyden-Möbius).
- Scapulohumeral (Erb's juvenile).

INHERITANCE

Autosomal recessive, with high sporadic incidence.

SIGNS AND SYMPTOMS

- Variable age of onset; childhood to early adult (present in second or third decade).
- Pelvic girdle usually involved first and to greater extent.
- Shoulder girdle often asymmetric.

DIAGNOSIS

Muscle biopsy shows dystrophic muscle changes. Dystrophin is normal.

MANAGEMENT

- Promote ambulation.
- Physiotherapy.
- Mildly progressive, life expectancy mid to late adulthood.

FACIOSCAPULOHUMERAL MUSCULAR DYSTROPHY

INHERITANCE

Autosomal dominant.

SIGNS AND SYMPTOMS

- Variable.
- Slow progression.
- Diminished facial movements: Inability to close eyes, smile, or whistle.
- Weakness of the shoulder girdle: Difficulty raising arms over head.
- Normal life span.

Dermatomyositis/Polymyositis

DEFINITION

- **Polymyositis** primarily affects skeletal muscle.
- **Dermatomyositis:** Skin eruption + myopathy.

Epidemiology

- Female > male.
- Age 5–14 years.

Signs and Symptoms

- Symmetric proximal muscle weakness.
- Violaceous rash—symmetric, erythematous rash on extensor surfaces, upper eyelids, and knuckles. Rash around eyes called *heliotrope rash*.
- Worrisome triad (not common):
  - Dysphagia.
  - Dysphonia.
  - Dyspnea.

Diagnosis

- ESR, serum CK, and aldolase reflect the activity of the disease.
- Electromyography (EMG) is used to distinguish myopathic from neuropathic causes of muscle weakness.

Treatment

- Prednisone.
- Intravenous immune globulin (IVIG), cyclosporine, or methotrexate in refractory cases.

Prognosis

Most children will recover in 1–3 years.

Connective Tissue Diseases

MARFAN SYNDROME

Definition

Genetic defect of genes coding for the connective tissue protein fibrillin.

Inheritance

Autosomal dominant.

Signs and Symptoms

- **Musculoskeletal:**
  - Tall stature.
  - Long, thin digits (arachnodactyly).
  - Hyperextensible joints.
  - High arched palate.
- **Cardiac:** Dilation of the aortic root.
- **Pulmonary**: Propensity to develop spontaneous pneumothorax.
- **Ocular:** Ectopia lentis—lens dislocation (which progresses over time).

EHLERS-DANLOS SYNDROME (EDS)

Definition

Group of genetically heterogenous connective tissue disorders.

Etiology

- Quantitative deficiency of collagen causing poor cross-linking of collagen.
- Autosomal dominant.

SIGNS AND SYMPTOMS

- Children with EDS are normal at birth.
- Skin hyperelasticity.
- Fragility of the skin and blood vessels.
- Joint hypermobility.
- Propensity for tissue rupture.

MANAGEMENT

- Symptomatic.
- Preventive.
- Prolonged wound fixation.
- Genetic counseling.

SCOLIOSIS

DEFINITION

More than 10-degree curvature of spine in the lateral plane due to the rotation of the involved vertebrae (see Figure 19-12).
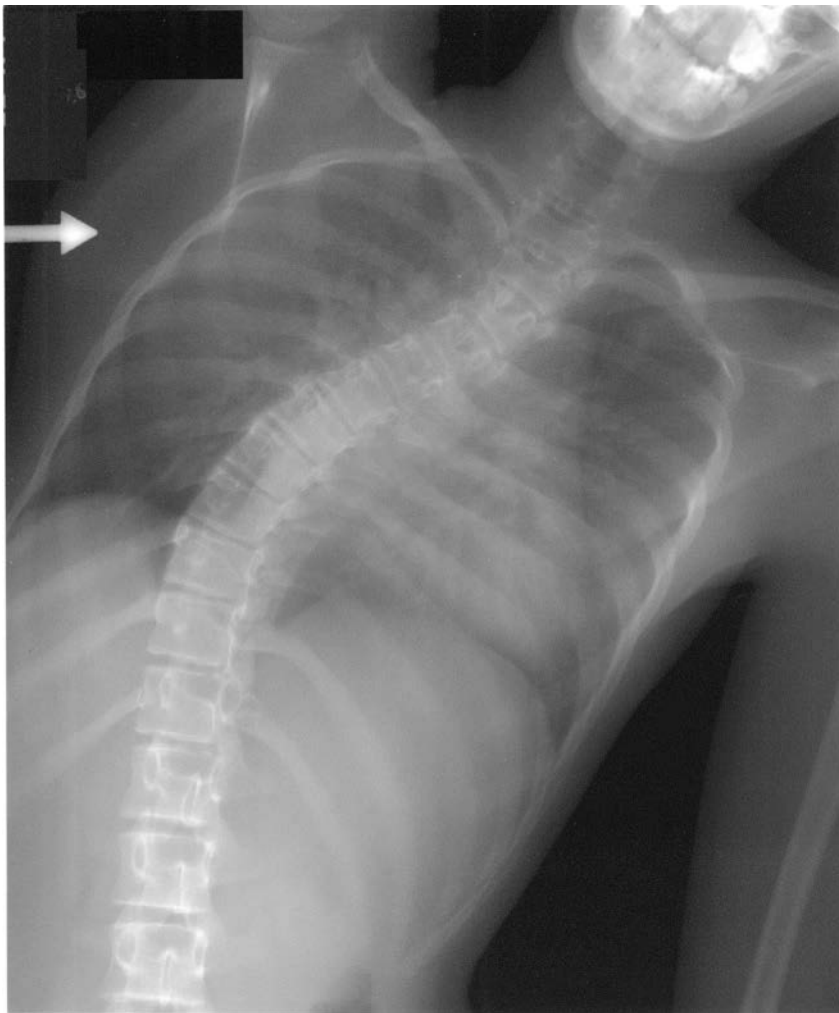
F I G U R E 1 9 - 1 2 .   **Radiograph of spine demonstrating marked scoliosis.**

ETIOLOGY

- Eighty percent of cases are idiopathic.
- Scoliosis is associated with:
  - Neurofibromatosis.
  - Marfan syndrome.
  - Cerebral palsy.
  - Muscular dystrophy.
  - Poliomyelitis.
  - Myelodysplasia.
  - Congenital vertebral anomalies (hemivertebrae, unilateral vertebral bridge).

EPIDEMIOLOGY

- Four to five times more common in girls.
- Age of onset: 9–10 years for girls, 11–12 years for boys.

SIGNS AND SYMPTOMS

- Usually asymptomatic.
- Severe curvature may lead to impairment of pulmonary function (restrictive lung disease).

DIAGNOSIS

- X-ray of entire spine in both the AP and lateral planes.
- To examine children, have the patient bend forward 90 degrees with the hands joined in the midline. An abnormal finding consists of asymmetry of the height of the ribs or paravertebral muscles on one side.

MANAGEMENT

Treatment depends on the curve magnitude, skeletal maturity, and risk of progression:
- Curve <20 degrees: Physical therapy and back exercises aimed at strengthening back muscles.
- Curve 20–40 degrees in a skeletally immature child: Orthopedic back brace. A back brace does not ↓ the curve, but prevents further curve progression.
- Curve >40 degrees: Spinal fusion to correct deformity.

PROGNOSIS

- Curve >60 degrees: Associated with poor pulmonary function. Large thoracic curves are associated with a shortened life span.
- Curve <40 degrees: Usually do not progress. Small curves are well tolerated.
- Risk of progression higher in younger childhood.

KYPHOSIS

DEFINITION

Posterior curvature of the spine.

ETIOLOGY

Scheuermann thoracic kyphosis is a structural deformity of the thoracic spine.

SIGNS AND SYMPTOMS

- Pain.
- Progressive deformity.
- Neurologic compromise.

EXAM TIP

Thirty percent of family members of patients with scoliosis are also affected. Siblings of affected children should be carefully examined.

WARD TIP

Screening for scoliosis should begin at age 6–7 years.

- Cardiovascular complaints.
- Cosmetic issues.

RADIOLOGY

- Diagnosis is confirmed on lateral radiographs.
- X-ray shows anterior wedging of at least 5 degrees of three or more adjacent thoracic vertebral bodies.

SPONDYLOLYSIS

DEFINITION

Fracture of the pars interarticularis due to repetitive stress to this area.

ETIOLOGY

Spondylosis occurs as a result of new bone formation in areas where the annular ligament is stressed.

TYPES

- **Congenital:** Cervical.
- **Acquired:** Lumbar, most often at L5 (85% of cases).

SIGNS AND SYMPTOMS

- Cervical pain.
- Low back pain, worse during the adolescent growth spurt and with spine extension.
- Radicular symptoms are not common.

DIAGNOSIS

Oblique x-ray view of the spine will show the characteristic "Scottie dog sign."

TREATMENT

- NSAIDs.
- Strength and stretching exercises.
- Lumbosacral back brace.

SPONDYLOLISTHESIS

DEFINITION

Anterior or posterior displacement of one vertebral body on the next due to bilateral pars interarticularis injury.

SIGNS AND SYMPTOMS

- A palpable "step-off" at the lumbosacral area.
- Limited lumbar flexibility.

DIAGNOSIS

Lateral x-ray views show displacement of one vertebral body from another.

MANAGEMENT

Treatment depends on grade of lesion:
- <30% displacement: No restrictions on sports activities, but requires routine follow-up.
- >50% displacement: In situ posterior spinal fusion or bracing.

WARD TIP

Spondylolysis is the most common cause of low back pain in adolescent athletes. This injury is most commonly seen in gymnasts, dancers, and football players.

EXAM TIP

Grade 1: <25% displacement
Grade 2: 25–50%
Grade 3: 50–75%
Grade 4: 75–100%
Grade 5: Complete displacement

EXAM TIP

Children at highest risk for diskitis:
- Immunocompromised
- Systemic infections
- Postsurgery

COMPLICATIONS

- Deformity.
- Disability.

DISKITIS

DEFINITION

- Pyogenic infection of the intervertebral disk space.
- An uncommon primary infection of the nucleus pulposus, with secondary involvement of the cartilaginous end plate and vertebral body.

ETIOLOGY

- Most present prior to 10 years of age.
- Spontaneous.

SIGNS AND SYMPTOMS

- Moderate to severe pain.
- Pain is localized to the level of involvement and exacerbated by movement.
- Radicular symptoms.

LABS

- MRI is the radiographic study of choice.
- Elevated ESR.

MANAGEMENT

- Intravenous antibiotics.
- Surgery is often not necessary unless abscess is identified.

Renal Osteodystrophy

DEFINITION

Bone diseases resulting from defective mineralization due to renal failure.

SIGNS AND SYMPTOMS

- Growth retardation.
- Muscle weakness.
- Bone pain.
- Skeletal deformities.
- Slipped epiphyses.

DIAGNOSIS

- Normal to ↓ serum calcium.
- Normal to ↑ phosphorus.
- ↑ alkaline phosphatase.
- Normal parathyroid hormone (PTH) levels.
- Radiographs of the hands, wrists, and knees show subperiosteal resorption of bone with widening of the metaphyses.

TREATMENT

- Low-phosphate formula.
- Enhance fecal phosphate excretion with oral calcium carbonate, an antacid that also binds phosphate in the intestinal tract.

WARD TIP

The lumbar spine is the most common site of involvement for diskitis.

WARD TIP

S. aureus is the most common organism causing diskitis.

WARD TIP

Plain radiographs are usually not helpful for early diagnosis of diskitis.

WARD TIP

In children, renal osteodystrophy resembles rickets.

■ The goals of treatment include normalization of the serum calcium and phosphorus levels and maintenance of the intact PTH level in the range of 200–400 pg/mL.

Osteochondritis Dissecans

DEFINITION

Avascular necrosis of bone adjacent to articular cartilage. Often occurs as a type of overuse injury.

SIGNS AND SYMPTOMS

■ Vague pain (typically in the knee or ankle).
■ With joint flexed, may be able to palpate defect below articular cartilage.
■ May present as a loose body in the joint.
■ Most common in the lateral portion of medial femoral condyle.

DIAGNOSIS

■ X-rays show characteristic appearance of subcondylar osteonecrosis.
■ MRI may be useful to confirm diagnosis.

TREATMENT

■ Children <11 years—typically observed with serial radiographs to assess healing.
■ Adolescents—excision of loose fragments if small. Replacement with fixation if large. Sometimes area can be drilled to promote revascularization and healing.

PROGNOSIS

Typically good with appropriate intervention.

Dermatologic Disease

Classification of Skin Lesions

PRIMARY SKIN LESIONS

- **Macule:** Flat, nonpalpable, <1 cm skin discoloration.
- **Patch:** Flat, nonpalpable >1 cm skin discoloration.
- **Plaque:** Elevated, flat-topped, >1 cm diameter.
- **Wheal:** Elevated, round or flat-topped area of dermal edema, disappears within hours.
- **Vesicle:** Circumscribed, elevated, fluid-filled, <1 cm diameter.
- **Bullae:** Circumscribed, elevated, fluid-filled, >1 cm, diameter.
- **Pustule:** Circumscribed, elevated, pus-filled.
- **Papule:** Elevated, palpable, solid, <1 cm diameter.
- **Nodule:** Elevated, palpable, solid, >1 cm.
- **Petechiae:** Red-purple, nonblanching macule, usually pinpoint, caused by extravasated red blood cells.
- **Purpura:** Red-purple, nonblanching macule, caused by extravasated red blood cells.
- **Telangiectasia:** Blanchable, dilated blood vessels.

SECONDARY SKIN LESIONS

- **Scale:** Accumulation of stratum corneum.
- **Crust (scab):** Dried serum, blood, or purulent exudate on skin surface.
- **Erosion:** Superficial loss of epidermis, leaving a denuded, moist surface; heals without scar.
- **Ulcer:** Loss of epidermis extending into dermis; heals with scar.
- **Scar:** Replacement of normal skin with fibrous tissue as a result of healing.
- **Excoriation:** Linear erosion produced by scratching.
- **Atrophy:** Thinning of skin.
- **Lichenification:** Thickening of epidermis with accentuation of normal skin markings.

Diagnostic Procedures Used in Dermatology

- **Diascopy:** Glass slide pressed firmly against red lesion—blanchable (capillary dilatation) or nonblanchable (extravasation of blood).
- **Gram stain:** Stains bacterial cell wall and divides bacteria into two main categories: Gram-positive and gram-negative; can be performed on body fluid and biopsies.
- **KOH prep:** Identifies fungi and yeast under microscope.
- **Tzanck smear:** Helps identify virally infected cells (typically herpes infection) from the base of a vesicle or ulcer under the microscope.
- **Scabies prep:** Skin scraping to identify mites, eggs, or feces under microscope.
- **Wood's lamp:** Tinea capitis will fluoresce green/yellow on hair shaft.
- **Patch testing:** Detects type IV hypersensitivity reactions (allergic contact dermatitis).

Papulosquamous Reactions

PSORIASIS (FIGURE 20-1)

DEFINITION

- Chronic, noninfectious, hyperproliferative inflammatory disorder.
- Polygenic, chronic, relapsing, T cell–mediated inflammatory skin disease.

ETIOLOGY

- Unknown, but with genetic predisposition.
- Triggering factors: Trauma, infection, and medications.

PATHOPHYSIOLOGY

↑ epidermal cell proliferation due to a shortened epithelial cell cycle.

EPIDEMIOLOGY

- Rarely presents at birth.
- One-third of cases of psoriasis present in <20 years old.

SIGNS AND SYMPTOMS

- **Classic:** Thick, silvery-scaled, sharply defined, pink plaques occurring on the scalp, elbows, and knee.
- Common locations: Scalp, elbows, knees, umbilicus, and diaper area in infants.
- Nails commonly involved—pitting, "oil spots," onycholysis, subungual hyperkeratosis.
- May be associated with arthritis (psoriatic arthritis).
- Inverse psoriasis: Located in body folds such as axilla, inguinal creases, behind ears.
- Guttate psoriasis: Small, guttate ("droplike") papules with scale, group A streptococcus frequently a trigger.

> **WARD TIP**
>
> Salmon-pink plaques with silvery scale. *Think: Psoriasis.*

FIGURE 20-1. Silvery scale plaque of psoriasis. (Reproduced, with permission, from Fauci KS, Kasper DL, Braunwald E, et al. *Harrison's Principles of Internal Medicine*, 17th ed. New York: McGraw-Hill, 2008:311.)
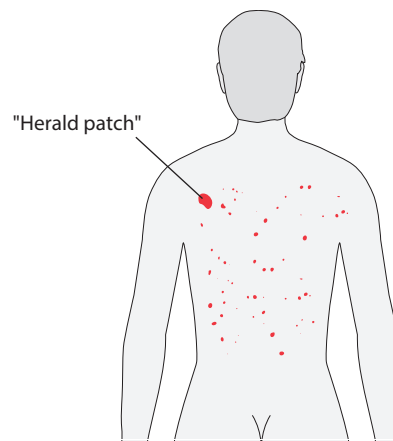
FIGURE 20-2. **Pityriasis rosea.** Note "Christmas tree" distribution of macules. Note "herald patch" that precedes other lesions.

DIAGNOSIS

- Clinical diagnosis.
- Potassium hydroxide (KOH) test and/or fungal culture to rule out fungal infection.

TREATMENT

- First line: Topical corticosteroids.
- Additional topicals: Coal tar, anthralin, synthetic vitamin D analogues (calcipotriene, calcitriol).
- If extensive or resistant—narrow band-ultraviolet B (NB-UVB) phototherapy, PUVA (psoralen and ultraviolet A [UVA]), retinoids, methotrexate, cyclosporine, TNF-alpha inhibitors.

PITYRIASIS ROSEA (FIGURE 20-2)

DEFINITION

Common, self-limited eruption of single herald patch followed by a generalized secondary eruption.

ETIOLOGY

Suspected infectious agents include HHV-6 or HHV-7.

EPIDEMIOLOGY

Affects children and young adults.

SIGNS AND SYMPTOMS

- Herald plaque—2- to 10-cm solitary, oval, erythematous, with collarette of scale.
- After several days to weeks, followed by a generalized eruption of multiple smaller, pink, oval, scaly patches over trunk and upper extremities following skin tension lines in a "Christmas tree" distribution.
- Can occur in an inverse form (extremities affected and trunk spared).
- Pruritus.

DIAGNOSIS

- Clinical.
- Rapid plasma reagin (RPR) to differentiate from syphilis if suspected, KOH to differentiate from fungal infection.

WARD TIP

Herald patch followed by a rash in a Christmas tree distribution (oriented parallel to the ribs). *Think: Pityriasis rosea.*

WARD TIP

Absence of herald patch does not exclude the diagnosis of pityriasis rosea.

WARD TIP

Must consider secondary syphilis in a sexually active adolescent if the rash involves palms and soles.

TREATMENT

- Self-limited, resolves in 6–12 weeks.
- Symptomatic: The goal is to control pruritus (baths, calamine, topical corticosteroids, oral antihistamines).

Eczematous Reactions

Eczema: Broad term used to describe several inflammatory skin reactions; used synonymously with dermatitis.

ATOPIC DERMATITIS (AD)

DEFINITION

Inflammatory skin disorder starting in early childhood.

ETIOLOGY

Complex interaction between impaired skin barrier, dysregulation of cutaneous inflammation, and environmental triggers.

EPIDEMIOLOGY

- Up to 11% of all children in the United States.
- Affects all ages, but onset usually in first 6 months of life.
- Two-thirds outgrow by age 10.
- Familial tendency and ↑ risk for other atopic disorders (allergic rhinoconjunctivitis, asthma, and food allergy).
- AD may be the initial manifestation of the "atopic march."

SIGNS AND SYMPTOMS

- Pruritic.
- Distribution varies with patient's age.
- Infantile—red, exudative, **crusty,** and **oozing** lesions primarily affecting face (especially cheeks), trunk, and extensor surfaces.
- Nose and **paranasal** areas often spared.
- Diaper area is also spared.
- Juvenile/adult: Dry, lichenified, pruritic plaques distributed over flexural areas (antecubital, popliteal, neck).
- Susceptible to secondary bacterial (*S. aureus*) and viral (molluscum contagiosum, herpes simplex virus) infections.

DIAGNOSIS

Clinical; supported by personal or family history of atopy.

TREATMENT

- Topical corticosteroids are the mainstay of therapy.
- Sensitive skin care (nonperfumed lotions, soaps detergents).
- Frequent moisturization to prevent dry skin.
- Avoid irritants such as wool, fragrances, and harsh cleansers.
- Oral antihistamines to manage itch.
- Bleach baths—to decrease bacterial colonization.
- Oral antibiotics *only* if clinical signs of secondary infection.
- **Avoid** oral corticosteroids: Patients become steroid dependent or rebound when discontinued.

WARD TIP

The herald patch may be mistaken for tinea corporis.

WARD TIP

Atopic dermatitis is part of the atopic triad: allergic rhinitis, asthma, and eczema.

WARD TIP

Skin colonization is common: 90% of atopic patients are carriers of *Staphylococcus aureus*.

CONTACT DERMATITIS

DEFINITION

Inflammatory skin reaction resulting from contact with an external agent.

ETIOLOGY

- Irritant: Non-immune based, direct cell injury from applied chemical.
- Allergic: Caused by a type IV hypersensitivity reaction.

SIGNS AND SYMPTOMS

- Sharply demarcated, erythematous vesicles and plaques at site of contact with agent.
- Chronic lesions may be lichenified.

DIAGNOSIS

- Clinical: Consider location, relationship to external factors, particular configurations.
- History alone can identify the sensitizing agent in only 10–20%.
    - Nickel.
    - Plant-associated (poison ivy).
- Patch testing to identify allergen.

TREATMENT

- Remove offending agent.
- Topical corticosteroids.

SEBORRHEIC DERMATITIS

DEFINITION

Chronic and recurrent skin inflammation occurring at sites with sebaceous gland activity, characterized by erythema and scaling.

ETIOLOGY

Unknown; however, *Malassezia furfur* has been implicated.

PATHOPHYSIOLOGY

Unknown.

EPIDEMIOLOGY

- Affects children and adults.
- Prevalence markedly increased in HIV+/AIDS patients.

SIGNS AND SYMPTOMS

- Children age 0–3 months: "Cradle cap"—greasy scales covering scalp, forehead, shoulders ("shawl distribution"), and folds (neck, axilla, inguinal creases).
- Adults: Flaking, greasy scales on erythematous background over scalp (dandruff), ears, eyelids (blepharitis), nasolabial fold, and central chest.

DIAGNOSIS

- Clinical.
- KOH or fungal culture to differentiate from fungal infection.

TREATMENT

- Symptomatic: Antiseborrheic shampoo (selenium sulfide), topical cortico-steroids (brief course) in the presence of inflamed lesions.
- Topical immunomodulatory agents (tacrolimus, pimecrolimus) >2 years.
- Consider **Langerhans cell histiocytosis** and HIV in the presence of chronic seborrhea.

Bullous Diseases

EPIDERMOLYSIS BULLOSA

DEFINITION

Inherited disorder of cell adhesion mechanisms characterized by trauma- or friction-induced skin blistering.

ETIOLOGY

Inherited mutation of cell adhesion proteins at the basement membrane zone.

EPIDEMIOLOGY

Can present from infancy to young adulthood.

SIGNS AND SYMPTOMS

Blistering and erosions at sites of trauma; distribution can be both local or generalized (see Figure 20-3).

DIAGNOSIS

- Skin biopsy for immunofluorescence microscopy.
- Genetic testing to confirm mutation.

TREATMENT

- Wound dressing with nonstick or nonadherent dressings.
- Infection prevention.
- Pain management.

FIGURE 20-3. **Pemphigus.** (Reproduced, with permission, from Weinberg S, Prose NS, Kristal L. *Color Atlas of Pediatric Dermatology*. New York: McGraw-Hill, 2008:180.)

FIGURE 20-4. **Erythema multiforme.** Note the many different-sized lesions. (Reproduced, with permission, from Stead LG, Stead SM, Kaufman MS. *First Aid for the Emergency Medicine Clerkship*, 2nd ed. New York: McGraw-Hill, 2006:356.)

ERYTHEMA MULTIFORME (FIGURE 20-4)

DEFINITION

Targetoid lesions presenting in an acral distribution.

ETIOLOGY

- Herpes simplex virus 1, less often herpes simplex virus 2.
- Less common viral causes: Epstein-Barr virus, varicella.
- EM-like rash can occur with Kawasaki disease.
- Idiopathic in 20–50%.
- Morphology: Target lesion (three zones: peripheral red ring, pale zone, and dusky, violaceous central zone).
- Central zone may blister.
- Mucosal lesions seen in 25–50% of cases.
- Heals in 2 weeks.
- Distribution: Symmetric palms, soles, extensor surface of the arms and legs.

PATHOPHYSIOLOGY

Unknown, likely hypersensitivity reaction.

EPIDEMIOLOGY

Older children and adults.

SIGNS AND SYMPTOMS

Pruritus or pain.

STEVENS-JOHNSON SYNDROME (ERYTHEMA MULTIFORME MAJOR)

DEFINITION

Widespread small blisters occurring on purple macules or flat atypical targets involving <10% of total body surface area.

ETIOLOGY

- Often medication-induced: Penicillin, sulfonamides, barbiturates, nonsteroidal anti-inflammatory drugs (NSAIDs), thiazides, phenytoin.
- Mycoplasma infection can lead to an SJS type presentation.

SIGNS AND SYMPTOMS

- Systemic prodrome: Fever, malaise, pharyngitis.
- Severe mucous membrane ulcers and sloughing (oral, vaginal, conjunctival).
- Targetoid lesion: Erythematous papule with central, dusky center which blisters.
- Ocular involvement (purulent uveitis/conjunctivitis) may result in scarring or corneal ulcers.
- May evince (+) Nikolsky sign.
- May evolve to toxic epidermal necrolysis.

TREATMENT

- Discontinue offending agent (if identified).
- Symptomatic and supportive care.
- Systemic steroids and IVIG can be used, but their efficacy is controversial.
- Observe closely for strictures developing upon mucous membrane healing.
- Mouthwashes, topical anesthetics, pain control.

> **EXAM TIP**
>
> **Nikolsky's sign:** Direct pressure applied to surface of bullas causes it to extend laterally.

TOXIC EPIDERMAL NECROLYSIS (TEN)

DEFINITION

↑ severe variant/progression of SJS.
- Blistering involving >30% body surface area.
- SJS/TEN Overlap: Blistering involving 10–30% body surface area.

SIGNS AND SYMPTOMS

- Widespread morbilliform rash or erythema with tenderness that quickly blisters.
- Absence of targetoid lesions.
- Sudden onset and generalization within 24–48 hours.
- Abrupt onset of fever and influenza-like symptoms.
- Pruritus, pain, tenderness, and burning.
- Full-thickness epidermal necrosis and a minimal to absent dermal infiltrate.
- Complications: Secondary skin infections, fluid and electrolyte abnormalities, prerenal azotemia.

ETIOLOGY

Hypersensitivity, triggered by medications listed above.

PATHOPHYSIOLOGY

Damage to basal cell layer of epidermis.

Diagnosis

Clinical; confirm by biopsy.

Treatment

- Removal and/or treatment of causative agent.
- Consider transfer to a burn unit.
- Fluid and electrolyte replacement.
- Role of IVIG or systemic steroids is controversial.
- Antibiotics (for secondary bacterial infection).

Cutaneous Bacterial Infections

IMPETIGO (FIGURE 20-5)

A 3-year-old girl had an upper respiratory infection for the past week. Two days ago, her parents noted a rash immediately under her nose. On examination, she is afebrile with multiple round and oval areas of erythema with golden-colored crusts. *Think: Impetigo.*

Impetigo is a highly contagious superficial skin infection that is limited to the epidermis. It is transmitted by direct contact. The nonbullous form is more common, which begins as a single papule that quickly becomes a vesicle. When this vesicle ruptures and the contents dry, characteristic honey or golden-colored crusts develops.

FIGURE 20-5. **Impetigo.** Note characteristic honey-colored crusted lesion, typically seen at corners of mouth and over face. (Reproduced, with permission, from Wolff K, Johnson RA, Suurmond D. *Fitzpatrick's Color Atlas & Synopsis of Clinical Dermatology*, 6th ed. New York: McGraw-Hill, 2009:599.)

DEFINITION

- Contagious, superficial, bacterial infection transmitted by direct contact.
- **Nonbullous in 70% of cases.**
- Bullous impetigo (most commonly affects neonates).

ETIOLOGY

- Non-bullous impetigo: *Staphylococcus aureus* and group A β-hemolytic *Streptococcus pyogenes* (GAS).
- Bullous impetigo: *Staphylococcus aureus.*

PATHOPHYSIOLOGY

Only epidermis is affected.

EPIDEMIOLOGY

- Common in children.
- Warm and humid climates.
- Crowded conditions.

SIGNS AND SYMPTOMS

- Mild burning or pruritus.
- Initial lesion is a transient erythematous papule or thin-roofed vesicle that ruptures easily and forms a honey-colored crust.
- Lesions can progress for weeks if untreated.

DIAGNOSIS

Clinical; can confirm with Gram stain and culture showing gram-positive cocci in clusters (*S. aureus*) or chains (GAS).

TREATMENT

- Remove crusts by soaking in warm water.
- Antibacterial washes (benzoyl peroxide).
- Topical antibiotic if disease is limited (Bactroban).
- Oral antibiotics if more severe.

> **WARD TIP**
>
> "Honey-colored crust" is classic for impetigo.

CELLULITIS

DEFINITION

Acute, deep infection of dermis and subcutaneous tissue.

ETIOLOGY

- *S. aureus* (rapidly changing epidemiology now identifies community-acquired methicillin-resistant *S. aureus* [CA-MRSA] as one of the common organisms).
- Group A β-hemolytic *S. pyogenes.*
- *Haemophilus influenzae* (children) less common due to immunization.

PATHOPHYSIOLOGY

- Precipitating factors include injury, abrasions, burns, surgical wounds, mucosal infections, bites, underlying dermatosis, and preexisting lymphatic stress.
- Risk factors include cancer, chemotherapy, immunodeficiency, diabetes, cirrhosis, neutropenia, and malnutrition.

EPIDEMIOLOGY

Any age.

Signs and Symptoms

- Erythematous, edematous, shiny area of warm and tender skin with poorly demarcated, nonelevated borders.
- Fever, chills, and malaise can develop rapidly.

Diagnosis

- Clinical; confirmed by Gram stain demonstrating gram-positive cocci in clusters or chains.
- Lesional and blood cultures only positive in 15% and 2% of cases, respectively.

Treatment

- In communities with high rates of MRSA, consider clindamycin or trimethoprim-sulfamethoxazole (TMP/SMX).
- TMP/SMX does not cover for GAS, so a cephalosporin can be added to TMP/SMX or, if MRSA is unlikely, may be used as monotherapy.
- Cefotaxime or ceftriaxone for *H. influenzae*.

ERYSIPELAS

Definition

- Variant of cellulitis.
- More commonly involves the upper dermis and superficial lymphatics (cf. involvement of deeper layers in cellulitis).
- An erysipelas-like presentation can be seen with erysipeloid (hands from handling infected food) and necrotizing fasciitis (medical emergency).
- Clear line of demarcation between involved and uninvolved tissue.
- Raised lesions above the surrounding normal skin.

Etiology

Group A streptococcus.

Epidemiology

↑ incidence in young children and adults.

Signs and Symptoms

- Local pain and tenderness.
- Acute onset of fever, malaise, and shivering may precede lesion.
- Well-demarcated, indurated, and elevated advancing border; less edematous (versus cellulitis).
- High morbidity if untreated.

Diagnosis

Clinical; Gram stain reveals gram-positive cocci in chains.

Treatment

Oral antibiotics (penicillin, cephalosporin, clindamcyin, vancomycin).

Toxin-Mediated Diseases

STAPHYLOCOCCAL SCALDED SKIN SYNDROME

Definition

Toxin-mediated blistering disease.

ETIOLOGY

- *S. aureus.*
- Epidermolytic toxins cleave desomoglein-1 causing separation of keratinocytes in the upper layers of the epidermis → superficial blistering.

PATHOPHYSIOLOGY

- Begins with local infection. Pathogen first colonizes nose, umbilicus, perioral region, perineum, or conjunctivae without causing clinical signs of infection.
- Produces exfoliatin and epidermolytic toxins that spread hematogenously to skin, resulting in blistering and sloughing of the epidermis.

EPIDEMIOLOGY

Newborns and infants (<2 years old).

SIGNS AND SYMPTOMS

- Skin is initially red and tender with flaccid bullae.
- Epidermis sloughs off and appears wrinkled, usually beginning around the mouth, neck, axillae, and groin.
- Becomes widespread within 24–48 hours, resembling scalding.
- (+) Nikolsky's sign.
- Self-limited in 5–7 days, though death can occur in neonates with extensive disease.

DIAGNOSIS

Clinical; skin biopsy in challenging cases. Infection confirmed by culture of colonized site (nose, eyes, throat) revealing gram-positive cocci.

TREATMENT

- Hospitalize newborns with extensive skin sloughing.
- Systemic antibiotics (oxacillin, dicloxacillin).
- Pain control.
- Intravenous (IV) fluids in severe cases.

> **WARD TIP**
>
> Culture of epidermolytic skin in staphylococcal scalded skin syndrome will not demonstrate the pathogen.

SCARLET FEVER

DEFINITION

Toxin-mediated disease characterized by sore throat, high fever, and erythema of the mucous membranes.

ETIOLOGY

Group A *Streptococcus.*

PATHOPHYSIOLOGY

Toxin-mediated.

EPIDEMIOLOGY

- Children.
- Untreated streptococcal infection of pharynx, tonsils, or wound.

SIGNS AND SYMPTOMS

- Fine pink-scarlet papules first appear on upper trunk 12–48 hours after onset of fever.
- As exanthem spreads to extremities, it becomes confluent and has a rough sandpaper-like texture.

- Fades in 4–5 days, followed by desquamation.
- Circumoral pallor.
- Linear petechiae evident in body folds (**Pastia's sign**).
- Pharynx is beefy red and tongue is initially white, but within 4–5 days the white coating sloughs off and tongue becomes bright red.

DIAGNOSIS

- Clinical; confirmed by culture from throat or wound.
- Rapid direct antigen tests detect GAS antigens.

TREATMENT

- Acetaminophen for fever and pain.
- Antibiotics (penicillin, macrolide, or cephalosporin).
- Follow-up recommended if history of rheumatic fever present.

Cutaneous Viral Infections

HAND, FOOT, AND MOUTH DISEASE

DEFINITION

Oral ulcers coupled with a macular or maculopapular eruption of the hands and feet.

ETIOLOGY

- Most commonly attributed to coxsackievirus A, though other enteroviruses have been linked to this syndrome.
- Virus transmitted via fecal-oral route.

EPIDEMIOLOGY

- More common in infants and children, though it can rarely occur in adolescents and adults.
- Higher incidence during the summer months.
- Outbreaks typically occur in daycares, summer camps, schools, etc.

SIGNS AND SYMPTOMS

- Oropharyngeal pain, difficulty feeding, fever.
- Viral prodromal symptoms, if present, may include fever, abdominal pain, diarrhea, or emesis.
- Oral lesions: Erythematous macules progressing to vesicles.
- Skin lesions: Football-shaped whitish vesicles with a rim of erythema involving the palms, soles, and buttock. Can be painful. Usually resolve within 1 week.

DIAGNOSIS

Clinical: Identification of the causative agent typically unnecessary.

TREATMENT

Supportive care; ensure adequate hydration.

VERRUCAE (WARTS)

DEFINITION

Viral infection of skin and mucous membranes spread by direct contact.

ETIOLOGY

Human papillomavirus (HPV).

EPIDEMIOLOGY

↑ incidence in atopic and immunocompromised patients.

SIGNS AND SYMPTOMS

- Tender if irritated.
- Types:
  - Verrucae vulgaris: Hands, fingers, knees; skin-colored papule.
  - Verrucae plantaris: Rough; over pressure points on plantar aspect of foot.
  - Verrucae planar: Flat; on face and dorsum of hands and fingers.
  - Condyloma acuminata: Anogenital warts.

DIAGNOSIS

Clinical—absence of normal skin lines and presence of black dots resembling thrombosed superficial blood vessels.

TREATMENT

Cryotherapy, topical keratolytic agents (e.g., salicylic acid), destructive agents (podophyllin), curettage and desiccation, topical imiquod.

HERPES GINGIVOSTOMATITIS (FEVER BLISTERS, COLD SORES)

DEFINITION

Painful vesicles involving the oral mucosa due to primary infection with herpes simplex virus type I.

ETIOLOGY

Herpes simplex virus (HSV) type 1.

PATHOPHYSIOLOGY

- Transmitted by direct contact with skin and mucous membranes.
- After primary infection, virus remains latent in a neural ganglion.
- Reactivation of latent virus results in recurrent disease, typified by several blisters at the lips.
- Recurrences become less frequent over time.

EPIDEMIOLOGY

- Primary infection affects children and young adults.
- ↑ incidence of infection in immunocompromised patients.

SIGNS AND SYMPTOMS

- Erythema and edema of gingiva and oral mucosa followed by vesicles on an erythematous base.
- Perioral lesions may develop.
- Erosions and crusted lesions form after a couple of days.
- Fever, malaise, headache, dehydration, and adenopathy may occur with primary infection.
- Prodrome of burning, tingling, or itching occurs with recurrent infection.
- Complications include dehydration, herpetic whitlow, or cutaneous HSV infection in areas of eczema in patients with atopic dermatitis, a condition termed *eczema herpeticum*.

EXAM TIP

HPV genotypes 6 and 11 are thought to cause 90% of condyloma acuminate cases, while genotypes 16 and 18 are most strongly associated with cervical dysplasia (precancerous).

WARD TIP

Herpetic whitlow (herpes-infected finger)—can occur in children with herpes gingivostomatitis secondary to sucking of fingers.
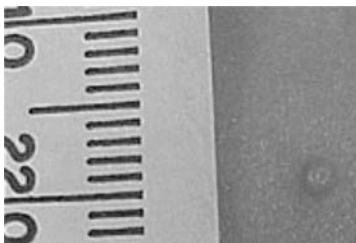
FIGURE 20-6. **Molluscum contagiosum.** (Used with permission from Danial Stuhlberg, MD, Utah Family Practice Residency, Provo, Utah.)

DIAGNOSIS

- Clinical.
- Confirmed by Tzanck preparation, revealing multinucleated giant cells.
- Viral culture or PCR of vesicle fluid.

TREATMENT

- Oral acyclovir, valacyclovir, or famciclovir ↓ viral shedding time and accelerate healing time. Consider if herpetic whitlow or at risk for severe disease.
- Suppressive therapy with acyclovir for more than six recurrences per year.

MOLLUSCUM CONTAGIOSUM (FIGURE 20-6)

DEFINITION

Self-limited, contagious, viral infection transmitted by direct contact.

ETIOLOGY

Molluscum contagiosum virus (poxvirus).

EPIDEMIOLOGY

- Affects children and sexually active adults.
- ↑ incidence in atopic and immunocompromised patients.

SIGNS AND SYMPTOMS

- Single or multiple, 2- to 5-mm, firm, umbilicated, skin-colored or pearly papules.
- Commonly found on face, eyelids, axillae, and anogenital region.
- Multiple lesions on face can be seen in the context of human immunodeficiency virus (HIV) infection.

DIAGNOSIS

Clinical.

TREATMENT

Curettage, cantharidin, cryosurgery, or observation as condition self-resolves.

Cutaneous Fungal Infections

TINEA (DERMATOPHYTOSES)

DEFINITION

- Group of noninvasive fungi that can infect keratinized tissue of epidermis, nails, and hair.
- Clinical presentation depends on anatomic site of infection and is named accordingly.

WARD TIP

Do not try to excise herpetic whitlow—opening the lesion will only serve to spill more virus onto surrounding skin and spread the infection.

WARD TIP

Umbilicated, pearly papules. *Think: Molluscum contagiosum.*

WARD TIP

Tinea corporis lesions are annular with peripheral scale and central clearing.

F I G U R E   2 0 - 7 .   **Tinea corporis (ringworm).**

ETIOLOGY

Trichophyton, Microsporum, Epidermophyton.

EPIDEMIOLOGY

Exacerbated by warm, humid climates.

SIGNS AND SYMPTOMS

- Tinea pedis ("athlete's foot").
- Tinea cruris ("jock itch"): Groin.
- Tinea corporis ("ringworm"): Body (see Figure 20-7).
- Tinea manuum: Hand.
- Tinea facialis: Face.
- Tinea capitis: Scalp.
- Tinea barbae: Beard/mustache area.
- Onychomycosis: Nails.

DIAGNOSIS

- Clinical presentation and history.
- KOH preparation reveals multiple, septated hyphae.
- Wood's lamp may reveal bright green fluorescence of hair shaft in some forms of tinea capitis.
- Fungal culture of affected area may demonstrate dermatophyte.

TREATMENT

- **Prevention:** Wearing well-ventilated shoes and clothing.
- Topical antifungal agents (imidazoles and terbinafine) for skin infection.
- Systemic antifungal agents for tinea capitis and onychomycosis (**griseofulvin**, terbinafine).

CANDIDAL SKIN INFECTIONS (CANDIDA)

DEFINITION

Superficial infection occurring in moist cutaneous sites.

WARD TIP

Griseofulvin can cause elevation of liver enzymes.
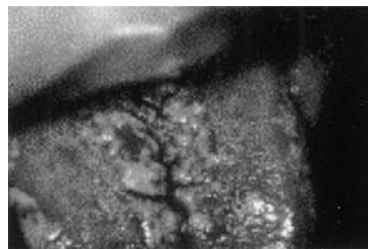
FIGURE 20-8. **Oral candidiasis (thrush).** (Reproduced, with permission, from Tay YK, Seow CS: What syndrome is this? Chronic mucocutaneous candidiasis. Pediatr Dermatol. 2001 Jul-Aug;18(4):353–5.)

ETIOLOGY

Candida albicans.

PATHOPHYSIOLOGY

Predisposing factors: Diabetes mellitus, obesity, immunosuppression, chronic debilitation, recent use of antibiotics.

SIGNS AND SYMPTOMS

- Pruritus and soreness.
- Confluent, bright red papules and pustules forming a sharply demarcated eroded plaque with pustular lesions at the periphery (satellite lesions).
- Most commonly found in the diaper area in children.
- Can occur in other intertriginous areas: axilla, inframammary creases.
- Oral form is thrush: Thick white plaque on tongue or inside of cheeks that can't be scraped off (Figure 20-8).

DIAGNOSIS

Clinical; confirmed by KOH preparation revealing pseudohyphae and budding spores with positive cultures of lesion.

TREATMENT

- Keep intertriginous areas dry.
- Topical antifungals (nystatin and azoles).
- Topical corticosteroids for symptomatic relief.

Infestations

LICE (PEDICULOSIS)

DEFINITION

1. Pediculosis corporis—body.
2. Pediculosis capitis—scalp hair.
3. Pediculosis pubis—pubic hair.

ETIOLOGY

1. *Pediculus humanus corporis.*
2. *Pediculus humanus capitis.*
3. *Pthirus pubis.*

WARD TIP

Thrush is a candidal infection of mucosal surfaces, presenting as creamy white, easily removable papules on an erythematous mucosal surface (see Figure 20-8).

WARD TIP

Diaper rash is often superinfected with *Candida*, which manifests as erythematous satellite lesions.

PATHOPHYSIOLOGY

Lice are obligate parasites, feeding on human blood.

EPIDEMIOLOGY

1. Poor hygiene.
2. Head-to-head contact, sharing hair items.
3. Sexual contact.

SIGNS AND SYMPTOMS

- Pruritus.
- Superficial bacterial infections may develop from scratching.
- Corporis—primary lesion is an intensely pruritic, small, red macule or papule with central hemorrhagic punctum on shoulders, trunk, or buttocks; secondary lesions include excoriations, wheals, and eczematous, secondarily infected plaques.

DIAGNOSIS

Nits detectable on hair/fibers.

TREATMENT

- Hot water laundering.
- Boil or dispose of implements such as combs.
- Comb hair and mechanically remove lice.
- Permethrin application—once, then again at 1 week (alternatives—pyrethrin, malathion).

SCABIES

A 4-year-old boy has been treated with hydrocortisone cream for eczema on and off for the last 3 years. Over the past 2 months, parents have noted a pruritic, papular rash that improves when hydrocortisone cream is used but returns when hydrocortisone is discontinued. On examination, he is afebrile with diffusely distributed papules on the trunk and extremities, concentrated in the intertriginous areas. Burrows are noted as well. *Think: Scabies.*

Scabies. It is a highly contagious disease caused by the mite *Sarcoptes scabiei* and spreads in households with intimate personal contact or sharing of inanimate object. Schoolchildren are especially at higher risk. Typical presentation is generalized, intense nocturnal itching, and classic sites are hairless areas with a thin stratum corneum (interdigital web spaces of fingers and toes, popliteal fossae, flexor surfaces of the wrists, and gluteal region). Presence of skin burrows is the most supportive finding. Definitive diagnosis is established by finding the scabies mites. The most effective topical treatment is 5% permethrin. One application is usually effective but a second treatment 1 week after the first application may be required.

ETIOLOGY

Female mite *Sarcoptes scabiei hominis.*

PATHOPHYSIOLOGY

- Pregnant female mite exudes keratolytic substance and burrows into the stratum corneum, depositing eggs and feces daily.
- Eggs hatch; larvae molt into nymphs, mature in 2–3 weeks, and repeat the cycle.

EPIDEMIOLOGY

- Physical contact with infected individual.
- Rarely transmitted by fomites, as isolated mites die within 2–3 days.

SIGNS AND SYMPTOMS

- Pruritus at initial infestation.
- First sign: 1- to 2-mm red papules, some of which are excoriated, crusted, or scaling.
- Threadlike burrows.
- Multiple types of lesions.
- Common locations in children and adults: Interdigital web space, axilla, wrists, ankles, buttock, belt area, and penis. Doesn't involve scalp or face.
- Infants are more likely to have nodules and papules located on palms, soles, scalp, and occasionally face.

DIAGNOSIS

Scraping for microscopic identification of mites, ova, and feces.

TREATMENT

- Permethrin, neck down, in children older than 2 years. Use on scalp only if scalp involvement; leave on 8–12 hours; may be repeated after 1 week.
- Permethrin to face and scalp in children less than 2 years old.
- Alternatives include sulfur ointment and oral ivermectin.

WARD TIP

Threadlike burrows are classic for scabies, but may not be seen in infants.

WARD TIP

Transmission of scabies mites is unlikely 24 hours after treatment.

Growths

INFANTILE HEMANGIOMA

DEFINITION

Benign vascular proliferation that is not fully formed at birth and grows within the first few months) (Figure 20-9).

ETIOLOGY/PATHOPHYSIOLOGY

Abnormal angiogenesis, potentially stimulated by localized hypoxia in utero.

EPIDEMIOLOGY

Approximately 4% of infants.

SIGNS AND SYMPTOMS

- Red papules or nodules that develop soon after birth, increases in size generally over the first 5–6 months of life and then slowly involutes over years (see Figure 20-10).
- If more than five infantile hemangiomas, there is a risk of hepatic hemangiomas.

FIGURE 20-9. **Port-wine stain seen in Sturge-Weber syndrome.** (Reproduced, with permission, from Wolff K, Johnson RA, Suurmond D. *Fitzpatrick's Color Atlas & Synopsis of Clinical Dermatology*, 5th ed. New York: McGraw-Hill, 2005:187.)
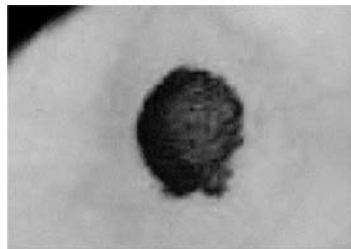
FIGURE 20-10. **Capillary hemangioma.**

TREATMENT

- Most resolve without treatment.
- Oral beta-blocker propranolol for hemangiomas that are disfiguring or impact function (i.e., oral feeding, breathing, vision).

MELANOCYTIC NEVUS (MOLE) (FIGURE 20-11)

DEFINITION

Benign proliferation of melanocytes, which can be classified according to location of clustering on histopathology: dermal-epidermal junction (junctional), dermis (dermal), or both (compound).

EPIDEMIOLOGY

Nevi usually arise in childhood, and peak during adolescence. Decreased development of new nevi seen in adulthood.
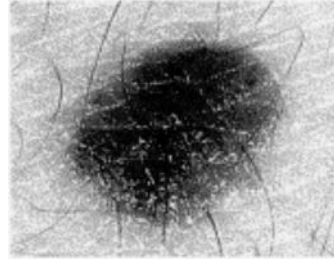
FIGURE 20-11. Melanocytic nevus. (Reproduced with permission from Wang SQ, Katz B, Rabinovitz H, et al: Lessons on dermoscopy. Compound congenital melanocytic nevus, Dermatol Surg. 2000 Apr;26(4):397–398.)

TREATMENT

- Serial observation for early recognition of premalignancy.
- Early excision of suspicious lesions.

MALIGNANT MELANOMA

DEFINITION

Malignant proliferation of melanocytes.

ETIOLOGY

May arise from normal-appearing skin or from preexisting mole or skin lesion.

PATHOPHYSIOLOGY

- Horizontal growth phase: Lateral extension within the epidermis and dermis.
- Vertical phase: Penetrates into dermis, greatly increasing risk of metastasis.

EPIDEMIOLOGY

- ↑ incidence in fair-skinned people and with sun exposure.
- Adolescents.
- Increased risk in patients with large congenital melanocytic nevi (measure >20 cm in diameter).

SIGNS AND SYMPTOMS

Characteristics of a mole suspicious for melanoma:
- Asymmetric.
- Border (irregular).
- Color (variegated and mottled).
- Diameter (>0.6 cm).
- Elevated.
- Enlarging.

DIAGNOSIS

Prognosis based on thickness of the primary tumor.

TREATMENT

- Surgical excision with margins at least 1 cm beyond borders, depending on depth of lesion.
- Close follow-up.

WARD TIP

Characteristics of mole suspicious for melanoma:
- Asymmetric
- Borders irregular
- Color uneven
- Diameter >0.6 cm
- Elevated
- Enlarging

Genetic Dermatology

XERODERMA PIGMENTOSUM

DEFINITION

Genetic defect in nucleotide excision repair mechanisms, predisposing to certain skin cancers.

ETIOLOGY

Autosomal recessive.

PATHOPHYSIOLOGY

Failure to repair ultraviolet-damaged DNA.

SIGNS AND SYMPTOMS

- Severe sensitivity to the sunlight leading to easily developed and intense sunburns.
- Predisposes patients to basal and squamous cell skin cancers.

TUBEROUS SCLEROSIS COMPLEX

DEFINITION

Heterogeneous, inherited neurocutaneous disorder involving multiple organ systems, often presenting with characteristic hamartomas.

ETIOLOGY

Autosomal-dominant mutation in either the *TSC1* (expresses hamartin) or *TSC2* (expresses tuberin) gene.

PATHOPHYSIOLOGY

Both proteins thought to exert a net inhibitory influence on the cell cycle; loss thereby leads to tumor formation.

SIGNS AND SYMPTOMS

- Dermatologic:
    - Ash-leaf spots: Hypopigmented lesions.
    - Angiofibromas (sebaceous adenoma): Red, vascular facial nodules.
    - Shagreen patches: Raised plaques on lower back with orange-peel texture.
- Neurologic:
    - CNS tumors (e.g., hamartomas, subependymal nodules, subependymal giant cell astrocytomas).
    - Seizures.
    - Impaired cognition.
- Cardiac rhabdomyomas.
- Renal angiomyolipomas.

NEUROFIBROMATOSIS TYPE 1 (NF1)

DEFINITION

- Inherited neurocutaneous disorder with at least two of the clinical features listed below:
    - At least 6 café-au-lait macules (CALMs).
    - Neurofibromas or a plexiform neurofibroma.

- Axillary or inguinal freckling.
- Optic glioma.
- Iris hamartomas (Lisch nodules).
- A distinctive bony lesion.
- First-degree relative with NF1.

ETIOLOGY

Autosomal-dominant mutation in the *NF1* gene (expresses neurofibromin).

PATHOPHYSIOLOGY

Neurofibromin is a GTPase activating protein that exerts a net inhibitory effect on the cell cycle. Reduced amounts of protein result in loss of this inhibition, resulting in variable clinical manifestations.

SIGNS AND SYMPTOMS

- Highly variable among different mutations.
- Typical progression: CALMs → Axillary/inguinal freckling → Lisch nodules → Neurofibromas.
- Dermatologic:
  - CALMs: Flat, uniformly hyperpigmented macules appearing in the first year of life.
  - Axillary/inguinal freckling. Appears at age 3–5 years.
  - Neurofibromas. May be discrete (nodular, cutaneous subtypes) or diffuse and disfiguring (plexiform subtype).
- Neurological:
  - Lisch nodules: Iris hamartomas, specific for NF1.
  - Optic gliomas.
  - Seizures.
  - Macrocephaly.
  - Impaired cognition.
- Skeletal:
  - Long bone dysplasia.
  - Pseudoarthrosis (Nonunion of two fractured bones; absence of healing).
- Soft tissue sarcomas.

Other Skin Conditions

HENOCH-SCHÖNLEIN PURPURA (FIGURE 20-12)

DEFINITION

Classic example of vasculitis in children.

ETIOLOGY/PATHOPHYSIOLOGY

- Immunoglobulin A (IgA) deposition in small vessel walls.
- Occurs most commonly following streptococcal or viral infection.

EPIDEMIOLOGY

Pediatric age group.

SIGNS AND SYMPTOMS

- Palpable purpura.
- Arthritis.
- Abdominal pain or GI bleeding.

DIAGNOSIS

Clinical; may biopsy.

WARD TIP

Palpable purpura is the classic sign of small-vessel damage.

FIGURE 20-12. **Henoch-Schönlein purpura.** (Reproduced, with permission, from Knoop KJ, Stack LB, and Storrow AB, et al. *Atlas of Emergency Medicine*. 3rd ed. New York: McGraw-Hill, 2010:429. Photo contributor: Lawrence B. Stack, MD.)

TREATMENT

- Usually benign, self-limited.
- Non-steroidal anti-inflammatory drugs.
- Monitor for renal dysfunction for months after diagnosis.

ACNE VULGARIS

DEFINITION

- Disorder of pilosebaceous glands.
- Develops in areas with the greatest concentration of sebaceous glands.

ETIOLOGY/PATHOPHYSIOLOGY

- Results from a combination of hormonal (androgens), bacterial (*Propionibacterium acnes*), and genetic factors.
- Initial pathology is microscopic microcomedo.

EPIDEMIOLOGY

Adolescents.

SIGNS AND SYMPTOMS

- Comedone: Plug of sebaceous and dead skin material stuck in the opening of a hair follicle; open follicle (blackhead) or almost closed (whitehead).
- Pustules, papules.
- Painful nodules and cysts if severe.
- Seborrhea of face and scalp (greasy skin).
- Depressed or hypertrophic scars may develop with healing.

DIAGNOSIS

Clinical; confirmed by presence of comedones.

TREATMENT

- Benzoyl peroxide wash.
- Topical antibiotics (clindamycin or erythromycin):
  - Oral tetracyclines (thought to exert both antibacterial and anti-inflammatory effects).
- Topical retinoid: ↑ cell turnover and prevent comedone development.
- Oral isotretinoin (Accutane) for severe, recalcitrant, nodular acne.
- Dermabrasion or laser for treatment of scars.

WARD TIP

Intestinal wall purpura can serve as a lead point for intussusception.

WARD TIP

Accutane is teratogenic, therefore **monthly pregnancy monitoring is required for females**.

DIAPER RASH

DEFINITION

Rash occurring in the diaper area.

ETIOLOGY

- Irritant contact dermatitis: Prolonged dampness, interaction of urine (ammonia) and feces with the skin.
- Candidal or bacterial secondary infection can occur.
- May be any other dermatologic condition in diaper distribution such as psoriasis, Langerhans cell histiocytosis, or a nutritional deficiency.

PATHOPHYSIOLOGY

Overhydration, friction, maceration, allergy, etc.

EPIDEMIOLOGY

Most children who wear diapers, to some degree.

SIGNS AND SYMPTOMS

- Red, scaly, fissured, eroded skin.
- Patchy or confluent.
- Involves the convex portion of the buttock (the part touching the diaper); candida involves the inguinal creases.
- Check for oral candidiasis if candida is present in the diaper area.

TREATMENT

- Keep infant dry, change diapers often.
- Ointments and thick barrier creams made with zinc oxide can protect the skin from irritation.
- Avoid powders, as they can injure infants' lungs if inhaled accidentally.
- Nystatin or other antifungal cream for yeast infection.

VITILIGO

DEFINITION

Disorder of skin depigmentation.

ETIOLOGY/PATHOPHYSIOLOGY

- Unknown, possibly autoimmune.
- Trauma may be associated with initiation of the lesions.

EPIDEMIOLOGY

Half of cases present before 20 years of age.

SIGNS AND SYMPTOMS

- Depigmented macules and patches.
- Predilection for areas of trauma (hands, knees, elbows, waistband).

DIAGNOSIS

Clinical, though melanocyte absence can be confirmed by a skin biopsy.

TREATMENT

- Phototherapy, e.g., narrow-band UVB therapy.
- Potent topical steroids or topical tacrolimus.

A 12-year-old boy with a history of multiple food allergies ate a candy bar given to him by a friend at school. He complained of throat discomfort and a rash. On examination, he is afebrile. He is wheezing. Multiple discrete erythematous papules are noted on trunk and extremities. *Think: Urticaria.*

Urticaria with or without angioedema is frequently seen in pediatric practice. Angioedema is due to an urticarial process that involves deeper layers of the skin. Acute urticaria is more common in children. History is often able to identify an inciting factor, especially if the hives occur shortly after ingestion of a food or drug. Common foods that cause urticaria are milk, eggs, peanuts, and shellfish. The mast cell is the mediator in the development of urticaria. These lesions are typically pruritic and erythematous, often showing central clearing. Systemic symptoms develop if it is associated with anaphylaxis.

DEFINITION

Allergic response → edema of the tissues.

ETIOLOGY/PATHOPHYSIOLOGY

Type 1 hypersensitivity reaction of immunoglobulin E (IgE) with mast cells causes the release of histamine, → vasodilation, ↑ vascular permeability, and axonal response.

EPIDEMIOLOGY

Can occur in response to a large number of entities—ingestion, contact, infectious agents, environmental factors, or genetic conditions.

SIGNS AND SYMPTOMS

- **Urticaria:** Well circumscribed, but can be coalescent, erythematous, raised lesions (wheals or welts) (see Figure 20-13). Individual lesions do not last more than 24 hours.
- **Angioedema:** Involves the deeper layers of skin, submucosa, and subcutaneous tissues.

FIGURE 20-13.   Urticaria.

TREATMENT

■ Usually self-limited.
■ Antihistamines.
■ Watch for signs of airway compromise (especially with angioedema).
■ Epinephrine for signs of anaphylaxis.

Neonatal Dermatologic Conditions

See Table 20-1.

HAIR LOSS

MOST COMMON ETIOLOGIES

■ Tinea capitis (see Cutaneous Fungal Infections).
■ Trichotillomania.
■ Alopecia areata.

TRICHOTILLOMANIA (HAIR PULLING)

DEFINITION

■ Traumatic hair pulling resulting in breaking of hair shafts at different lengths.
■ Can also involve eyebrows or eyelashes.

ETIOLOGY

■ Habitual.
■ Sign of psychiatric disorder.
■ Reaction to stress.

T A B L E 2 0 - 1 . Neonatal Dermatology

CONDITION	ETIOLOGY	APPEARANCE	RESOLUTION
Sebaceous hyperplasia	Maternal and infant hormones	Shiny yellow papules	A few weeks
Acne neonatorum	Inflammatory reaction to *Malassezia*	Similar to minor acne vulgaris	Peaks at 2 months
Milia	Retention of dead skin and oily material in hair follicles	White papules on face	Within first month
Erythema toxicum neonatorum	Unknown, possible hypersensitivity	Blotchy red spots with overlying white or yellow papules or pustules	A few days
Dermal hypermelanosis (previously known as "Mongolian spots")	Melanocytes arrested in migration from neural crest to epidermis	Congenital, blue-gray macules, especially in nonwhite infants	First few years of life, though some never disappear

SIGNS AND SYMPTOMS

- Patchy hair loss of scalp (often on side of dominant hand).
- Loss of eyebrows, eyelashes.
- Close examination of hair demonstrates hair shafts broken at different lengths.

TREATMENT

- Behavioral modification.
- Consider psychiatry/psychology referral.

ALOPECIA AREATA (FIGURE 20-14)

DEFINITION

Non-scarring hair loss.

ETIOLOGY

Immune-mediated loss of hair. Course can be relapsing/remitting in some children.

SIGNS AND SYMPTOMS

- Smooth circular areas of hair loss.
- Exclamation point hairs.

TREATMENT

- High rates of spontaneous resolution/regrowth within 12 months.
- In some cases, steroids (systemic, topical, or local injection).

DERMATOLOGIC MANIFESTATIONS OF SOME INFECTIOUS DISEASES

See Table 20-2.

FIGURE 20-14. Alopecia areata of scalp: Solitary lesion. A sharply outlined portion of the scalp with complete alopecia without scaling, erythema, atrophy, or scarring. Empty follicles can still be seen on the involved scalp. The short, broken-off hair shafts (so-called exclamation point hair) appear as very short stubs emerging from the bald scalp. (Reproduced, with permission, from Wolff K, Johnson RA, Suurmond D. *Fitzpatrick's Color Atlas & Synopsis of Clinical Dermatology*, 5th ed. New York: McGraw-Hill, 2005:956.)

T A B L E   2 0 - 2 .   Dermatologic Manifestations of Some Infectious Diseases

Rubella (German measles)	▪ Pink macules and papules, initially on face and spread inferiorly within 24 hours ▪ Rash lasts 3 days, i.e., the "3-day measles"
Measles (rubeola, a paramyxovirus)	▪ Erythematous macules and papules initially along hairline, spreading inferiorly within 2–3 days, fade within 4–6 days ▪ Koplik's spots: Bluish-white papules on erythematous base appear on day 2 of fever, over buccal mucosa, adjacent to second molars
Rocky mountain spotted fever (*Rickettsia ricketsii*)	▪ 2–6 mm erythematous macules that appear peripherally on wrists, forearms, ankles, palms, and soles ▪ Spreads to trunk, proximal extremities, and face within 6–18 hours ▪ Evolves to deep-red papules and petechiae over 1–3 days ▪ Within 2–4 days, exanthema is no longer blanchable
Erythema infectiosum (fifth disease; Parvovirus B19)	▪ "Slapped cheeks"—red papules coalesce on face ▪ Lacey rash on buttocks and upper arms that spreads ▪ Palms and soles may be involved
Meningococcemia (*Neisseria meningitidis*)	▪ Discrete, petechiae, and pink or purpuric macules, and papules over trunk, extremities, and palate
Gonococcemia (*Neisseria gonorrhoeae*)	▪ Erythematous macules over arms and legs evolve into hemorrhagic, painful pustules within 2–3 days
Syphilis (*Treponema pallidum*)	▪ Primary: Painless ulcer termed a chancre with indurated borders ▪ Secondary: Multiple, "ham-colored" papules scattered symmetrically over trunk, palm, soles, and genitals; condyloma lata—soft, flat-topped, pink papules in anogenital region ▪ Tertiary: Gummas—brown, firm plaques on body
Lyme disease (*Borrelia burgdorferi*)	▪ Erythema chronicum migrans—expanding, erythematous, annular plaque with central clearing
Bacterial endocarditis	▪ **Osler's nodes:** Tender, violaceous subcutaneous nodules on palms and soles ▪ **Janeway lesions:** Multiple, hemorrhagic, nontender macules on fingers and toes ▪ Subungual splinter hemorrhages ▪ Multiple petechiae on upper chest and mucous membranes
Kawasaki disease (etiology unknown)	▪ Erythematous macules and plaques appear in a stocking-and-glove distribution 1–3 days after onset of fever ▪ Spreads to involve trunk and extremities within 2 days, lasts an average of 12 days

Dermatologic Manifestations of Systemic Disease

See Table 20-3.

TABLE 20-3. Dermatologic Manifestations of Systemic Disease

Sturge-Weber syndrome	■ **Port-wine stain:** Capillary malformation in a segmental distribution on the face ■ Port wine stains are fully formed at birth, persist into adulthood and can thicken over time ■ Appear as a well-demarcated red to purple patch
Dermatomyositis	■ **Heliotrope sign**: lilac color and edema of upper eyelids ■ **Gottron papules**: Pink to violaceous, flat-topped papules on the knuckles ■ **Shawl sign:** Violaceous erythema of the neck, shoulders, and upper back ■ Calcinosis cutis: Calcification in the skin common in juvenile dermatomyositis ■ **Samitz sign:** Ragged and frayed cuticles
Systemic lupus erythematosus	■ **Malar rash:** Erythematous plaques on the cheeks ■ Photosensitivity ■ Oral ulcers ■ **Discoid lupus**: Annular erythema, atrophy, scale, and hypo- or hyperpigmentation; common locations: hard palate, conchal bowl, head and neck
Obesity, metabolic syndrome	■ **Acanthosis nigricans:** Velvety, hyperpigmented plaques; occur on the neck, axilla, groin
Peutz-Jeghers syndrome	■ **Lentigines:** Hyperpigmented macules on nose, mouth, oral cavity, hands, and feet

NOTES

Psychiatric Disease

Psychiatric Examination of Children

- Consult multiple sources:
    - Child: Young children usually report information in concrete terms but give accurate details about their emotional states.
    - Parents, teachers, child welfare, and social services workers.
- Methods of gathering information from children:
    - Play, stories, drawing.
    - Kaufman Assessment Battery for Children (K-ABC): Intelligence test for ages 2½ to 12.
    - Wechsler Intelligence Scale for Children–Revised (WISC-R): Intelligence quotient (IQ) for ages 6–16.
    - Peabody Individual Achievement Test (PIAT): Tests academic achievement.

Intellectual Disability (ID)

See Neurologic Disease chapter.

Learning disability

See Neurologic Disease chapter.

Behavioral Disorders

DEFINITION

Behavioral disorders include oppositional defiant disorder and conduct disorder.

OPPOSITIONAL DEFIANT DISORDER (ODD)

A 9-year-old boy's mother has been called to school because her son is defiant toward the teacher and does not comply with her requests to follow the rules. His parents report similar scenarios at home, and he often becomes argumentative with them. *Think: Oppositional defiant disorder.*

A certain degree of oppositional behavior may be normal in childhood. However, normal defiance should not **impair significant social relationship or academic performance**. Children with this condition have substantially impaired relationships with parents, teachers, and peers. They might not show oppositional behavior in the pediatrician office. The diagnosis is therefore based on reports from the parents or teachers. Attention deficit/hyperactivity disorder (ADHD) and other mood disorders may coexist.

DIAGNOSIS

- *Diagnostic and Statistical Manual of Mental Disorders,* 5th ed. (DSM-V) definition: Recurrent pattern of argumentative, defiant, vindictive, and hostile behavior ≥6 months.
- Consistent pattern of disobedience toward parent or teacher.
- Four or more of the following criteria are usually present:
  - Loses temper.
  - Argues with adults.
  - Refuses to follow rules.
  - Deliberately annoys others.
  - Does not take responsibility for mistakes or behavior.
  - Sensitive, touchy, easily annoyed.
  - Angry, resentful.
  - Spiteful, vindictive.
  - Behavior causes impairment in social and academic functioning.
- Rule out other causes of clinical presentation.

PATHOPHYSIOLOGY

Low self-esteem, low frustration tolerance, often with comorbid substance abuse.

EPIDEMIOLOGY

- Prevalence: 2–16%.
- May be a precursor of a conduct disorder.
- ↑ incidence of substance abuse, mood disorders, ADHD.

TREATMENT

- Behavioral therapy, problem-solving skills.
- Early intervention is more effective than waiting for a child to grow out of it.
- Parental management training.

CONDUCT DISORDER

A 9-year-old boy's mother has been called to school because her son has been hitting other children and stealing pens. She reports that he often pokes their family cat with sharp objects. *Think: Conduct disorder.*

This disorder involves a variety of problematic behaviors, including oppositional and defiant behaviors and antisocial activities such as lying, stealing, running away, and physical violence. It is a pattern of behavior that violates the basic rights of others. The basic problem is a chronic conflict with parents, teachers, and peers. It is two to three times more common in boys. Conduct disorder is difficult to treat, and these behaviors are more likely to persist into adulthood.

DIAGNOSIS

- Chronic conflict with parents, teachers, or peers.
- A repetitive and persistent pattern of behavior that involves violation of the basic rights of others or of social norms and rules, with at least three of the following in 1 year:
  - Aggression toward people and animals.
  - Destruction of property.

WARD TIP

Temper tantrums and breath holding are manipulative behaviors.

WARD TIP

ODD can be a developmental antecedent to conduct disorder. The former does not involve violation of the basic rights of others.

EXAM TIP

Oppositional Defiant Disorder versus Conduct Disorder.

- ▪ Deceitfulness or theft.
- ▪ Serious violation of rules.
- ▪ The change in behavior causes significant impairment in social, academic, or occupational functioning.
- ▪ A closely linked behavior is juvenile delinquency, which is a tendency to break the law or engage in illicit behavior.

ETIOLOGY

- ▪ Lack of empathy is an important risk factor.
- ▪ Involves genetic and psychosocial factors.

EPIDEMIOLOGY

- ▪ High risk of developing antisocial personality disorder in adulthood.
- ▪ ↑ incidence of ADHD, learning disorders, mood disorders, substance abuse, and criminal behavior in adulthood.

TREATMENT

Multimodal:
- ▪ Structured environment, firm rules, consistent enforcement.
- ▪ Psychotherapy: Behavior modification, problem-solving skills.
- ▪ Adjunctive pharmacotherapy may help: Antipsychotics, lithium, selective serotonin reuptake inhibitors (SSRIs).

Attention Deficit/Hyperactivity Disorder (ADHD)

An 11-year-old boy's mother has been called to school because her son has not done his homework. He claims that he did not know about the assignments. He interrupts other kids and is often restless in his seat and gets up during class. His parents report that he cannot sit still at the dinner table. *Think: **ADHD—inattentive, and hyperactive in at least two settings.***

DEFINITION

Three types predominantly:
- ▪ Inattentive.
- ▪ Hyperactive-impulsive.
- ▪ Combined: Most children have the combined type.

DIAGNOSIS

- ▪ Six or more than six of the following symptoms present for more than 6 months by age 12:
  - ▪ **Inattention**: Problems listening, concentrating, paying attention to details, organizing tasks, easily distracted, forgetful.
  - ▪ **Hyperactivity-impulsivity**: Unable to inhibit impulses in social behavior, → blurting out, interrupting, fidgeting, leaving seat, talking excessively.
  - ▪ **Combined subtype**: Six or more symptoms of inattention and hyperactivity-impulsivity.
  - ▪ Behavior inconsistent with age and development.
  - ▪ Impairment interferes in two or more settings (social, academic, occupational, etc).

- The above may lead to:
    - Difficulty getting along with peers and family.
    - School underachievement secondary to poor organizational skills.
    - Poor sequential memory, deficits in fine motor skills.
- Medical conditions and sleep conditions must be ruled out before a diagnosis of ADHD is made.
- Important to rule out other situations that can trigger ADHD-type behaviors, such as death in the family, divorce, inner ear infection that causes temporary hearing problems, anxiety or depression, learning disability, child abuse.

ETIOLOGY

- Genetic predisposition and environmental factors (including family dysfunction).
- Perinatal complications, maternal nutrition and substance abuse, obstetric complications, viral infections.
- Neurochemical/neurophysiologic factors (e.g., lead poisoning).
- Psychosocial factors, including emotional deprivation and parental anxiety and inexperience.

PATHOPHYSIOLOGY

- Catecholamine hypothesis: A decrease in norepinephrine metabolites.
- Hypodopaminergic function, low levels of homovanillic acid.

EPIDEMIOLOGY

- Prevalence: 5% among young and school-age children.
- Male to female ratio 3:1.
- ↑ incidence of mood disorders, personality disorders, conduct disorder, and ODD.
- Between 25% and 75% continue to have ADHD in adulthood. Adults with ADHD can have difficulties at work and in their personal lives.

TREATMENT

- Pharmacotherapy:
    - **First line**: Psychostimulants such as methylphenidate (Ritalin), dextroamphetamine, pemoline.
    - **Second line**: Atomoxetine.
    - Atypical antipsychotics: On the rise; work by blocking dopamine.
    - Clonidine: Caution when using in combination with methylphenidate.
- Non-pharmacotherapy:
    - Behavior modification, cognitive behavioral therapy, group therapy.
    - Lifestyle modification: Increased physical activity has been shown to affect executive function, attention, behavior such as impulsivity.
    - Parental counseling: Positive reinforcement, firm nonpunitive limit setting, reduced external stimulation.

Pervasive Developmental Disorders (PDDs)

DEFINITION

- Group of conditions that involve problems with social skills, language, and behaviors.
- Apparent early in life with developmental delay involving multiple areas of development.

WARD TIP

The three cardinal signs of ADHD:
- Inattention
- Hyperactivity
- Impulsivity

Symptoms **must** be present in two or more situations and in multiple domains for a diagnosis of ADHD.

WARD TIP

Stimulants used appropriately for ADHD do not cause addiction.

EXAM TIP

ADHD in teens and adults can be linked to increased risk-taking behavior and depression.

EXAM TIP

There is a high degree of comorbidity in children with ADHD to also have conduct disorder or ODD.

- Include autistic disorder, Asperger syndrome (no longer classified as its own distinct disorder), Rett syndrome, and childhood disintegrative disorder.
- Pervasive developmental disorder not otherwise specified (PDD-NOS; atypical autism): Diagnosed when criteria are not met for any of the above.

TREATMENT

- There is no cure, but goal of treatment is to manage symptoms and improve social skills.
- Remedial education.
- Behavioral therapy.
- Neuroleptics such as haloperidol to control self-injurious and aggressive behavior and mood lability.
- SSRIs to help control stereotyped and repetitive behaviors.

AUTISM SPECTRUM DISORDER

A 3-year-old boy is brought in by his parents because they think he is deaf. He shows no interest in them or anyone around him and speaks only when spoken to directly. He often lines his toys up in a straight line. Hearing tests are normal. *Think: Autism.*

Autism is a spectrum of behaviors that include abnormalities in social interactions, aberrant communication, and restricted repetitive and stereotyped behaviors. The onset is before age 3 years. Speech is typically delayed or may regress. It is often associated with intellectual disability.

Spectrum of pervasive developmental disorders characterized by various degrees of impaired social interaction and communication and repetitive, stereotyped patterns of behavior.

DIAGNOSIS

1. Deficits in all three forms of social communication and interaction:
   - Social-emotional reciprocity (back and forth conversation).
   - Nonverbal communication (abnormal eye contact, can't understand gestures).
   - Maintaining and understanding relationships evident in difficulty or lack of ability or interest in making friends.
2. Repetitive, restrictive behavioral patterns or activities:
   - Echolalia or repetitive movements, unwavering adherence to routine/sameness.
   - Increased or decreased response to sensory input (a sound, excessive touching objects).
3. Symptoms must be present in early development, must impair life either in early or later development.

ETIOLOGY

- Genetic predisposition (88% concordance rate in monozygotic twins, 33% in dizygotic twins).
- Prenatal neurologic insult.
- Immunologic and biochemical factors.

PATHOPHYSIOLOGY

- Neuroanatomic structural abnormalities.
- Abnormalities in dopamine and serotonin system: ↑ in serotonin.

EPIDEMIOLOGY

- Prevalence: >1:100
  - Has been increasing for unknown reasons, may be due to increased screening, understanding and diagnostic accuracy. Other environmental causes have been proposed.
- 4:1 male to female.
- Significant comorbidity with fragile X syndrome, tuberous sclerosis, intellectual disability, and seizures.

TREATMENT

- No curative treatment.
- Supportive modalities.
  - Early intervention: Free services for less than 3 years focusing on strengthening and achieving developmental milestones.
  - Applied behavioral analysis (ABA): Encourages positive behaviors and discourages negative behaviors.
- Medication to decrease harmful or negative sequelae (self-injury, irritability, etc.): Risperadone is FDA approved, other non-FDA-approved medications include SSRI, TCA, stimulant, anti-convulsants.

RETT SYNDROME

> A 4-year-old girl with prior history of severe intellectual disability is brought in for evaluation. She had been developing **normally until 18 months of age**, when she began regressing intellectually and her head circumference plateaued. She **wrings her hands and has ataxia and marked loss of gross motor skills**. *Think: Rett syndrome.*
>
> Rett syndrome is a pervasive developmental disorder. It is a genetic disorder in which developmental arrest typically occurs between 6 and 18 months. Parents may report gross motor development delay, disinterest in play, and loss of eye contact. Hand wringing is a hallmark of this condition. Rapid deterioration may occur. This diagnosis should be considered in a previously healthy child with normal development who develops deceleration of head growth.

DIAGNOSIS

- Normal pre- and perinatal development until between 6 and 18 months of age.
- Normal head circumference at birth, but ↓ rate of growth between the ages of 6 and 18 months.
- Loss of previously learned purposeful hand skills between the ages of 6 and 30 months, followed by the development of stereotyped hand movements.
- Early loss of social interaction, usually followed by subsequent improvement.
- Problems with gait or trunk movements: 50% of females are not ambulatory.
- Severely impaired language and psychomotor development.
- The diagnosis is also supported by a positive mutational analysis of *MECP2*.
- Prone to seizure disorders and gastrointestinal complaints (constipation).

EPIDEMIOLOGY

- Classically restricted to females; males are beginning to be recognized due to genetic testing.
- The gene for Rett syndrome is located on the X chromosome.

PROGNOSIS

- Females can live up to 40 years of age.
- Currently, there is no cure.

WARD TIP

Computed tomography (CT) and magnetic resonance imaging (MRI) in autistic disorder may be normal or may show ventricular enlargement; polymicrogyria; histolocially may show small, densely packed, immature cells in the limbic system and cerebellum.

WARD TIP

Those with autistic disorder and who do speak exhibit echolalia, pronoun reversal, inappropriate cadence or intonation, impaired semantics, and failure to use language for social interaction.

EXAM TIP

Generally, autistic disorders are more common in boys except Rett syndrome (more common in girls).

Tic Disorders

TICS

- Sudden, repetitive, stereotyped movements (motor tics) and utterances (phonic tics).
- Most common motor tics involve the face and head (e.g., blinking of eyes).
- Examples of vocal tics include coprolalia (repetitive speaking of obscene words) and echolalia (exact repetition of words).

TOURETTE SYNDROME

A 13-year-old boy has had **uncontrollable blinking** since he was 9 years old. Recently, he has noticed that he often involuntarily makes a **barking noise** that is embarrassing. *Think: Tourette syndrome.*

It is characterized by motor and phonic (or vocal) tics. Tics are defined as involuntary, sudden, intermittent, repetitive movements (motor tics) or sounds (phonic tics). Comorbidities, such as ADHD and obsessive-compulsive disorder, are common. The age of onset is before 18 years but most children show readily identifiable symptoms by age 7 years.

DIAGNOSIS

- Two motor tic + 1 vocal tic for >1 year, onset <18 years old.
  - Motor tics: Blinking, shrug shoulder, head jerk.
  - Vocal tics: Clear throat, yell word/phrase, hum.

EPIDEMIOLOGY

- Commonly associated with obsessive-compulsive disorder (OCD) and ADHD.
- Three times more common in boys.
- Onset usually between the ages of 7 and 8 years.

ETIOLOGY

- Genetic: 50% concordance rate in monozygotic twins, 8% in dizygotic.
- Neurochemical: Impaired regulation of dopamine in the caudate nucleus.

TREATMENT

- Supportive treatment is the mainstay of therapy: Psychobehavioral therapy, education, and reassurance.
- Pharmacotherapy only when symptoms interfere with functioning: Alpha agonist (clonidine, guanfacine) or atypical + typical antipsychotics.

Elimination Disorders

ENURESIS

DIAGNOSIS

- Lack of involuntary urinary continence ≥5 years old (or the equivalent developmental level).
- Occurs at least twice a week for at ≥3 consecutive months.

WARD TIP

Tics in Tourette syndrome may be consciously repressed for short periods of time.

WARD TIP

Children become adept at covering up their tics. For example, a child might cough to mask his or her tic of clearing his or her throat.

WARD TIP

When a child presents for evaluation of tics, it is imperative to look for comorbid symptoms of ADHD and OCD.

- Types:
    - **Primary**: Child never established continence.
    - **Secondary**: Child has established continence in past (commonly between 5 and 8 years old) consistently for at least 6 months.
- Rule out the influence of a medical condition (e.g., urethritis, diabetes, seizures) or medications.

ETIOLOGY

- Genetic predisposition.
- Physical factors: Small bladder, low nocturnal levels of antidiuretic hormone (ADH).
- Delayed or stringent toilet training.
- Psychosocial stressors.

EPIDEMIOLOGY

Prevalence: 5–10% among 5-year-olds, 3–5% among 10-year-olds
- Nocturnal enuresis is more common in males.
- Diurnal (daytime only) is more common in females.

SIGNS AND SYMPTOMS

Urination during the day, night, or both.

TREATMENT

- **First line for nocturnal enuresis:**
    - Behavior modification therapy (e.g., buzzer to wake up child when wetness is detected).
    - Pharmacotherapy: Desmopressin.

Additional Environmental Changes
- Changing routine, e.g., no liquids after dinner; urinate before going to bed.
- Enlist child in cure, offer positive reinforcement, do not punish.

> **WARD TIP**
>
> Most cases of enuresis spontaneously remit by age 7. Nighttime enuresis may persist and be normal into adolescence and even into adulthood.

ENCOPRESIS

DIAGNOSIS

- Involuntary or intentional stooling into inappropriate places (e.g., clothing or floor).
- Behavior must occur at least once a month for ≥3 months, starting at 4 years old.
- Rule out the influence of a medication or a general medical condition (e.g., hypothyroidism, lower gastrointestinal problems, dietary factors).

ETIOLOGY

- Anxiety about defecating in a particular place.
- A more generalized anxiety in response to stressful environmental factors.
- Oppositional behavior.
- Physiologic conditions: Lack of sphincter control; constipation with overflow incontinence is most common.

EPIDEMIOLOGY

- Prevalence: 1% in 5-year-old children (less common than enuresis).
- Incidence ↓ with age.
- More common in males than females.
- Associated with other conditions such as conduct disorder and ADHD.

Treatment

- Determine if underlying medical cause.
  - Majority of encopresis cases involve constipation. Stool softeners are often used, and encourage dietary changes (more fiber and appropriate fluid intake), to promote soft, easy-to-pass stool.
- Behavioral modification: Choose a specific time every day to attempt bowel movement.
- Psychotherapy, family therapy, and behavioral therapy.
- Enlist child in cure, positive reinforcement; do not punish.

Mood Disorders

- Depressive disorders can be classified into three types:
  - Major depressive disorder (MDD).
  - Dysthymic disorder (DD).
  - Depressive disorder not otherwise specified (NOS).

MAJOR DEPRESSIVE DISORDER (MDD)

Definition

- Pathologic sadness or despondency, not explained as a normal response to stress, that causes impairment in function.
- Recurrent condition that generally continues into adulthood.

Etiology/Pathophysiology

- Genetic predisposition.
- Catecholamine hypothesis: Depression is caused by a deficit of norepinephrine at nerve terminals throughout the brain.
- Cortisol hypothesis: Larger quantities of cortisol metabolites in blood and urine, abnormal diurnal variation.

Epidemiology

- 2% prevalence in children; 4–8% in adolescents.
- 15–20% incidence in adolescents.
- Incidence rises in postpubertal, girls > boys.
- Comorbidities: Anxiety/panic disorders, OCD, eating disorders, substance abuse, borderline personality disorder, ADHD, and ODD.
- Up to 15% of patients with depression attempt or contemplate suicide each year.
- Can persist into adulthood.

Diagnosis

- Five of the following signs for ≥2 weeks:
  - Depressed mood most of the day.
  - Loss of interest in activities.
  - Sleep disturbance (insomnia or hypersomnia) nearly every day.
  - Weight change or appetite disturbance.
  - ↓ concentration.
  - Suicidal ideation.
  - Psychomotor agitation or retardation.
  - Fatigue or loss of energy.
  - Feelings of worthlessness or inappropriate guilt.
- Always rule out other causes of the clinical presentation (e.g., hypothyroidism, nutritional deficiency, chronic infection/systemic disease, substance abuse).

WARD TIP

Fifty to sixty percent of individuals with a single depressive episode can be expected to have a second episode.

WARD TIP

Electroencephalography (EEG) in depression shows ↓ slow-wave (delta) sleep, shortened time before onset of rapid eye movement (REM), and longer duration of REM.

WARD TIP

In suspected cases of depression, be sure to look for other signs or risk factors such as school failure or family history of mental health disorders.

WARD TIP

A combination of treatments for depression may be necessary. Childhood depression should be treated with behavior modification before medication.

TREATMENT

- If suicidal or homicidal, admit to the hospital.
- If there is no harm risk to patient or others:
  - Biopsychosocial approach, cognitive behavior therapy (CBT), individual and/or group therapy, family intervention.
- If failed non-pharmacological treatment, start SSRIs (TCAs have risk of lethal overdose—look for convulsions, coma, and cardiac arrhythmias in toxicity).
- For severe, medication-resistant depression (or catatonia syndrome): Electric shock therapy.
- For adolescents, CBT and SSRIs appear to be most effective.

Persistent Depressive Disorder (Dysthymia)/Chronic Depression

- Depressed mood, more days than not, for ≥1 year.
  - Two of the following symptoms: Appetite disturbance, sleep disturbance, fatigue, low self-esteem, poor concentration, difficulty making decisions, or feelings of hopelessness.
  - No manic, hypomanic, or disturbance better explained by schizophrenic behavior.

Unspecified Depressive Disorder

Clinically significant depressive symptoms that cause distress or impairment in functioning, but do not meet full criteria for depressive disorder. Can be used where physician does not have sufficient information to make diagnosis of depression (e.g., emergency room setting).

SUICIDE

RELEVANT DEFINITIONS

- **Suicidal ideation:** With or without a plan.
- **Suicide gesture:** For attention, without intent for death.
- **Suicide attempt:** Intention for death.

ETIOLOGY

- Suicide is a complex human behavior with biologic, sociologic, and psychological roots.
- Psychiatric disorders: Correlations of suicidal behavior and mood or disruptive disorders, substance abuse, and personality disorders (borderline personality disorder).
- Environmental factors: Stressful life events; family disruption due to death or separation, illness, birth, or siblings; peer pressure; physical or sexual abuse.
- Parental influence: Psychiatric illness, substance abuse, violence, physical or sexual abuse.

EPIDEMIOLOGY

- Third leading cause of death for young adults age 10–19.
- Attempted suicides account for 6% of deaths in 10- to 14-year-olds and 11% of deaths in 15- to 19-year-olds.
- Of the 1–2% of those who attempt suicide, 10% will eventually complete the act.
- Boys attempt suicide less often but boys are more successful (girls tend to choose less lethal methods like overdose, cutting; boys will choose firearms, hanging).
- The rate of suicide is higher in Alaskan, Asian-American, and Native-American youth.
- **Risk factors:** Look for psychiatric disorders, prior attempts, family clustering of suicides, substance use/abuse, history of sexual abuse, or serotonin abnormalities.

WARD TIP

Use of antidepressant medications, particularly SSRIs, in adolescents may ↑ risk of suicidal thoughts and behaviors during initial weeks due to disinhibition.

EXAM TIP

One percent of suicide gestures are lethal.

EXAM TIP

Thirty to seventy percent of suicides occur with significant alcohol or drug abuse. Substance abuse disinhibits the individual to complete the act.

EXAM TIP

Suicide attempters: Female, younger, history of depression, alcoholism, personality disorder, impulsive, no planning, low lethality, drug overdose.

EXAM TIP

Suicide completers: Male, older, history of depression, alcoholism, schizophrenia, careful planning, high lethality, firearms.

ASSESSMENT

- Assess signs and symptoms, correlate with other clinical variables such as psychiatric and substance abuse history, gender, age, race, prior history of suicide attempts, and recent traumatic life events.
- **Key questions:** Are you having any thoughts about harming yourself or taking your life? Have you developed a plan? What is your plan?

TREATMENT

- Immediate hospitalization; remove all potentially lethal items.
- Psychotherapeutic intervention, trustful atmosphere, coping strategies; remove motivation for suicide; involve parents and relatives, guidance counselor.
- Pharmacotherapy depends on the accompanying diagnosis.

Violent Behavior

EPIDEMIOLOGY

- Homicide is the second leading cause of death among 15- to 19-year-olds and the leading cause of death in African-American adolescents.
- Rates of homicide are higher in males than in females.
- Death by firearm homicide is highest in the 15- to 24-year-old age group.

RISK FACTORS

- Look for clinical entities associated with violent behavior such as intellectual disability, moderate to severe language disorder, learning disorder, ADHD, mood disorders, anxiety disorders, personality disorders, conduct disorders, and ODD.
- Other risk factors: Substance abuse, gang involvement, history/exposure to domestic/child abuse, and access to firearms.

SCREENING

Ask about recent involvement in physical fights, carrying a weapon, firearms in household, concerns that an adolescent has about his/her safety, past episodes of trauma, and social problems in school or neighborhood.

Substance Abuse

EPIDEMIOLOGY

- Alcohol and cigarettes are the most prevalent drugs among school-age young adults.
- Marijuana is the most commonly reported illicit drug used.
- The prevalence of substance abuse varies according to age, gender, geographic region, race, and other demographic factors.

SIGNS AND SYMPTOMS

See Table 21-1 for signs and symptoms of intoxication and withdrawal due to substances of abuse.

T A B L E 2 1 - 1 . Substances of Abuse—Intoxication and Withdrawal

Substance	Intoxication/Overdose	Withdrawal
Alcohol	↓ fine motor control Impaired judgment and coordination Ataxic gait and poor balance Lethargy, difficulty sitting upright Respiratory depression **Rx:** Benzodiazepines, Folate, Thiame, Vitamin B12	Irritability, insomnia, disorientation, tremor, diaphoresis (6–24 hours) Alcoholic hallucination (1–2 days) Delirium tremens (2–5 days)—generalized tonic-clonic seizures
Sedative-hypnotics (benzodiazepines, barbiturates)	Drowsiness, slurred speech Incoordination, ataxia Mood lability, impaired judgment Nystagmus Respiratory depression, coma, death **Rx:** Benzodiazepines—flumazenil (careful, may precipitate seizures); barbiturates—alkalinize urine; both—activated charcoal	Autonomic hyperactivity Insomnia, anxiety, tremor Nausea, vomiting Delirium, hallucinations Seizures—may be life-threatening
Stimulants (cocaine, amphetamines)	Euphoria, sweating, chills, nausea Autonomic instability, cardiac arrhythmias Psychomotor agitation, dilated pupils Vasoconstriction—MI, CVA **Rx:** Benzodiazepines (haloperidol if severe)	Not life-threatening Dysphoric "crash," depression, anxiety Hunger, craving Constricted pupils
Opioids (heroin, codeine, morphine, methadone, meperidine)	Drowsiness, slurred speech Nausea, vomiting, constipation Constricted ("pinpoint") pupils Seizures Respiratory depression **Rx:** Naloxone/naltrexone, methadone taper	Not life-threatening Dysphoria, insomnia Lacrimation, rhinorrhea Yawning, weakness, muscle aches Sweating, piloerection, dilated pupils Nausea, vomiting Rx: Clonidine, methadone taper
Hallucinogens (mushrooms, mescaline, LSD)	Perceptual changes, papillary dilation Tachycardia, palpitations Tremors, incoordination **Rx:** "Talk down", Benzodiazepines for agitation	May have flashbacks later due to reabsorption of lipid stores
PCP (hallucinogen)	Violence, recklessness, impulsivity Impaired judgment, nystagmus, ataxia Hypertension, tachycardia Muscle rigidity, high pain tolerance Seizures, coma **Rx:** Benzodiazepines, acidify urine	As with other hallucinogens, flashbacks may occur
Marijuana (THC)	Euphoria, impaired concentration Mild tachycardia Conjunctival injection Dry mouth, ↑ appetite	No withdrawal syndrome, but mild irritability, insomnia, nausea, and ↓ appetite may occur in heavy users

TABLE 21-1. Substances of Abuse—Intoxication and Withdrawal (*continued*)

SUBSTANCE	INTOXICATION/OVERDOSE	WITHDRAWAL
Inhalants	Impaired judgment, belligerence, impulsivity Perceptual disturbances, slurred speech Ataxia, dizziness Nystagmus, tremor, hyporeflexia Lethargy, euphoria, stupor, coma Respiratory depression, cardiac arrhythmias	Irritability, nausea, vomiting, tachycardia Occasional hallucinations
Caffeine	Anxiety, insomnia, twitching Flushed face, rambling speech GI disturbance, diuresis	Headache, nausea, vomiting, drowsiness Anxiety, depression
Nicotine	Restlessness, insomnia, anxiety ↑ GI motility	Dysphoria, anxiety, irritability, insomnia ↑ appetite, craving

CVA, cerebrovascular accident; GI, gastrointestinal; LSD, lysergic acid diethylamide; MI, myocardial infarction; PCP, phencyclidine; Rx, treatment; THC, tetrahydrocannabinol.

TREATMENT

- Non-pharmacologic: Group therapy, narcotics anonymous.
- Hospitalizations may be necessary for acute withdrawal.
- Alcohol abuse: Rule out medical complications, start benzodiazepine for withdrawal symptoms, and give thiamine before glucose to prevent Wernicke encephalopathy.

Anxiety Disorders

SEPARATION ANXIETY DISORDER

DEFINITION

- Excessive anxiety beyond that expected for the child's developmental level related to separation or impending separation from the attachment figure for more than 1 month.
- Separation anxiety is normal until age 3–4 years.

EPIDEMIOLOGY

- Prevalence: 4% of school-age children.
- Males and females are affected equally.

ETIOLOGY

Contribution by parental anxiety/excessive concern expressed.

SIGNS AND SYMPTOMS

- May refuse to sleep alone or go to school.
- May complain of physical symptoms in order to avoid anxiety-provoking activities (somaticization).
- Become extremely distressed when forced to separate, and may worry excessively about losing their parents forever.

TREATMENT

- Family therapy.
- Supportive psychotherapy.
- Low-dose antidepressants.

OBSESSIVE-COMPULSIVE DISORDER (OCD)

DEFINITION

- **Obsessions:** Persistent, intrusive thoughts, images, impulses involuntarily intruding into consciousness. Common themes are contamination and fear of harm to self or others.
- **Compulsions:** Actions due to a perceived internal obligation to follow certain rituals and rules.

DIAGNOSIS

Obsession and/or compulsions that cause significant impairment in social, academic, or vocational functioning.

ETIOLOGY

Genetic predisposition, higher concordance among monozygotic versus dizygotic twins.

EPIDEMIOLOGY

High comorbidity with ADHD + tic disorders.

SIGNS AND SYMPTOMS

- Preoccupied with details, rules, lists, order, organization, or schedules, resulting in loss of the goal of activity.
- Perfectionism that prohibits task completion.
- Social impairment secondary to preoccupation with work and level of productivity.
- Overconscientious, scrupulous, and inflexible about matters of morality, ethics, or values.
- Unable to discard objects of no worth or sentimental value.
- Preference to work as an individual and not in a group.
- Miserly spending in order to save for future catastrophes.
- Inflexible, rigid, stubborn.
- Characteristics must be ego-dystonic and functionally disruptive versus ego-syntonic and functionally adaptive in OCD.

TREATMENT

- Long-term therapy is required.
- Behavioral therapy such as self-observation, extinction, operant conditioning, and modeling.
- Pharmacotherapy:
    - First-line agents are SSRIs (i.e., fluoxetine, fluvoxamine, paroxetine, sertraline).
    - Clomipramine is a second-line agent.

SELECTIVE MUTISM

DEFINITION

Not speaking in certain situations (e.g., school).

EXAM TIP

Habit reversal: Substituting another, more benign behavior for the previous habit.

Epidemiology

- Onset usually around age 5 or 6.
- Girls > boys.
- May be preceded by a stressful life event.

Treatment

Supportive psychotherapy, behavior therapy, family therapy.

Gender Dysphoria

Diagnosis

- Marked difference between the gender assigned to the individual and how the person expresses/experiences gender for ≥6 months.
- This discrepancy causes significant stress and functional impairment in social, academic, and personal settings.

Epidemiology

- Prevalence: 1 in 30,000 males, 1 in 100,000 females.
- Coexisting separation and/or generalized anxiety disorder or depression is common.
- ↑ risk of suicide.
- Onset for boys is usually between ages 2 and 4; less clear for girls because cross-gender behaviors are more often tolerated in girls.

Signs and Symptoms

For genetic men: Overidentification with the mother, overtly feminine behavior, little interest in usual male pursuits, peer relationships primarily with girls.

- Persistent discomfort with his or her sex.
- Reflected in a combination of the following:
  - Stated desire to be or that he or she is the other gender.
  - Wearing clothes appropriate to the opposite gender.
  - Persistent role-playing or fantasies of being the opposite gender.
  - Interest in the habits of the opposite gender.
  - Preference for playmates of the opposite gender.

Treatment

General support in accepting patient's desired gender, through psychotherapy, hormone therapy, or surgery.

Eating Disorders (EDs)

Definition

Two subtypes:
- Restricting—limiting any oral intake.
- Binge eating/purging—binge eating or purging for 3 months.

ANOREXIA NERVOSA

A 16-year-old girl has a 6-month history of amenorrhea and a 25-lb weight loss. She is thin, with Tanner stage 4 development of breasts and pubic hair. She also reports constipation and feeling bloating. When you ask about her weight loss she states that she is "overweight." *Think: Anorexia nervosa.*

Anorexia nervosa is an eating disorder that is characterized by **weight loss, and psychiatric disturbance reflected as distorted body image**. Common presenting symptoms include **constipation, intolerance to cold, dry skin, and hair loss**. It predominantly affects females. Anorexia nervosa is associated with multiple hormonal abnormalities resulting in **amenorrhea**. Electrolyte abnormalities such as **hyponatremia, hypokalemia, hypophosphatemia**, and hypoglycemia may be present.

DIAGNOSIS

- Restriction of energy intake relative to requirement, leading to significant low body weight (BMI < 18.5) in context of age, sex, developmental trajectory, and physical health.
- Even though underweight, an intense fear of gaining weight.
- Disturbance in self-perception of body weight or lack of insight into the seriousness of physical condition.

ETIOLOGY

- Genetic predisposition (6–10% of female relatives of anorexic patients have the condition, twin studies confirm).
- Psychological need to control, perfectionism.
- Desire to conform to society's ideal of beauty.
- Stressful life events such as leaving home for college or death in the family.

PATHOPHYSIOLOGY

- A primary hypothalamic disturbance secondary to ↑ corticotropin-releasing factor.
- Central neurotransmitter dysregulation affecting dopamine, serotonin, and norepinephrine.
- Reduced norepinephrine activity and turnover.
- Endocrine abnormalities, ↑ growth hormone levels, loss of cortisol diurnal variation, reduced luteinizing hormone (LH), follicle-stimulating hormone (FSH), impaired response to luteinizing hormone–releasing hormone (LHRH), abnormal glucose tolerance test.

EPIDEMIOLOGY

- Predominance in females (female-to-male ratio 3:1).
- One percent prevalence among women.
- Bimodal onset at 14 and 18 years, but cases of earlier onset are continuing to rise.
- More common in industrialized countries.
- Incidence has ↑ over the past two decades.
- Common in individuals participating in ballet, gymnastics, and modeling.
- About half of anorexia patients have comorbid anxiety disorders, including obsessive-compulsive disorder and social phobia.

SIGNS AND SYMPTOMS

- Extreme dieting, special diets such as vegetarianism.
- Refusal to eat meals with family members or in public.

EXAM TIP

The most common cause of death in anorexia nervosa is cardiac arrhythmias due to electrolyte disturbances, particularly hypokalemia.

WARD TIP

Electrocardiography (ECG) in anorexia nervosa may show low-voltage T-wave inversion and flattening, ST depression, supraventricular or ventricular arrhythmias, and/or prolonged QT intervals.

- Preoccupation with food and its preparation.
- Denial of hunger.
- Obsessive interest in physical exercise.
- Abuse laxatives, diuretics, or stimulants in an effort to enhance weight loss.
- Multiorgan involvement: Amenorrhea, hypothermia, constipation, low blood pressure, bradycardia, lanugo, hair loss, petechiae, pedal edema, dry skin, osteopenia.
- Electrolyte abnormalities: Alkalosis, hypokalemia.
- Lab abnormalities: Leukopenia, elevated liver function tests (LFTs), elevated triglycerides, carotenemia.

TREATMENT

- Anorexic patients deny health risks associated with their behavior, making them resistant to treatment.
- Individual and family psychotherapy: Target abnormal and destructive thought processes.
- Behavior modification techniques to restore normal eating behavior, set specific weight goals.
- Nutritional rehabilitation: Restore nutritional state and weight.
- Pharmacologic therapy (SSRIs have been used successfully).

BULIMIA NERVOSA

A 15-year-old girl has bilateral parotid gland swelling and erosion of the posterior aspect of the dental enamel of her upper incisors. She reports frequent vomiting after her meal. *Think: Bulimia nervosa.*

Bulimia nervosa is characterized by recurrent episodes of binge eating defined as the rapid consumption of a large amount of food in a reasonably short period of time. The hallmark of bulimia is a fear of not being able to stop eating when the binge is in progress. Self-induced vomiting and excessive exercise are the compensatory behaviors. Parotid enlargement, dental problems, and abrasions of knuckles are due to biting down on them during self-induced vomiting. The typical age of presentation is during the teenage years.

DIAGNOSIS

- Recurrent episodes of eating within a 2-hour period of larger-than-normal proportions accompanied by a sense of lack of control over actions (binge eating).
- Episodes occur ≥ 1 a week for 3 months.
- Recurrent compensatory behavior in order to prevent weight gain—self-induced vomiting, laxatives, diuretics, enemas, excessive exercise.
- Body shape and weight is the basis of self-evaluation.
- Does not occur exclusively during episodes of anorexia nervosa.

ETIOLOGY

Genetics, environment (stress), psychological, and cultural influences.

PATHOPHYSIOLOGY

- A primary hypothalamic disturbance secondary to ↑ corticotropin-releasing factor.
- Central neurotransmitter dysregulation affecting dopamine, serotonin, and norepinephrine.
- Reduced norepinephrine activity and turnover.
- Endocrine abnormalities, low triiodothyronine (T_3), high T_3 receptor uptake (T_3RU), impaired thyrotropin-releasing hormone (TRH) responsiveness, abnormal dexamethasone suppression test.

EPIDEMIOLOGY

- Predominantly found in women (4% prevalence).
- Predominant in whites.
- More common in industrialized countries.
- Culturally dependent.

SIGNS AND SYMPTOMS

- Secretive binge-eating and purging behaviors.
- Abuse laxatives, diuretics, or stimulants in an effort to enhance weight loss.
- Obsessive interest in physical activity.
- Physical manifestations include parotid gland enlargement, dental caries, scars on dorsum of fingers (due to teeth scraping during self-induced vomiting).
- Laboratory abnormalities include dehydration, hypokalemia, hypochloremia, hypomagnesemia, elevated blood urea nitrogen (BUN), and amylase.

TREATMENT

Group therapy is the most effective treatment.

BING EATING DISORDER

- Binge eating at $\geq 1\times$ a week for ≥ 3 months.
- Marked distress regarding binge eating.
- Bing eating episodes associated with ≥ 3 of the following:
- Eating much more rapidly than normal.
    - Eating until feeling uncomfortably full.
    - Eating large amounts of food when not hungry.
    - Eating alone out of embarrassment over how much one is eating.
    - Feeling disgusted with oneself, depressed, or guilty after overeating.
- Not associated with purging (self-induced vomiting) or compensatory behavior to lose weight (laxative or exercise).

OTHER SPECIFIED FEEDING AND EATING DISORDER

DEFINITION

Abnormal eating behaviors or exhibits characteristics of other eating disorders without meeting all criteria. Examples include:
- Meets all criteria for anorexia nervosa except weight falls within normal range.
- Meets all criteria for bulimia nervosa or binge eating disorder but does not meet duration/frequency criteria.
- Night eating syndrome.
- Purging disorder.
- Unspecified feeding and eating disorder (does not fall in any of the above categories).

RUMINATION

DIAGNOSIS

- Repeated regurgitation and rechewing of food for a period of at least 1 month following a period of normal functioning.
- Other medical, psychiatric conditions (including other eating disorders) have been ruled out.

EXAM TIP

Rumination comes from the Greek root, *ruminare*, meaning "to chew the cud."

ETIOLOGY

- Adverse psychosocial environment.
- Individuals with intellectual disability.

PATHOPHYSIOLOGY

- Unsatisfactory mother–infant relationship that causes the infant to seek an internal source of gratification.
- Positive reinforcement when attention follows rumination.
- Negative reinforcement when rumination reduces anxiety.

EPIDEMIOLOGY

Highest prevalence in normal infants and intellectually disabled adults.

SIGNS AND SYMPTOMS

- Presents with "spitting up" or frequent vomiting.
- Effortless regurgitation, does not involve retching.
- Infants are irritable and hungry between episodes of regurgitation.
- Malnutrition, weight loss, failure to thrive.
- Up to 25% mortality rate.

TREATMENT

- Counseling to improve parent–child dynamics.
- Behavioral intervention.
- Aversive techniques—noxious stimulus are paired with rumination.
- Nonaversive techniques—differential reinforcement or other incompatible responses.
- In infants, the disorder frequently remits spontaneously.

PICA

DIAGNOSIS

- Persistent eating of nonnutritive substances for ≥1 month (e.g., clay, dirt, etc.).
- The eating of nonnutritive substances is inappropriate to the level of development.
- Behavior is not culturally sanctioned.
- Rule out other psychiatric disorders.

ETIOLOGY

- Intellectual disability.
- Vitamin or mineral deficiencies (e.g., iron deficiency anemia, particularly in pregnancy).
- Poverty, neglect, lack of parental supervision, developmental delays.
- Cultural belief.

EPIDEMIOLOGY

- In children aged 18 months to 2 years, the ingestion and mouthing of non-nutritive substances is normal behavior.
- Most common during 2 and 3 years of age.
- The prevalence ↑ with the severity of intellectual disability.

SIGNS AND SYMPTOMS

- Presenting complaint—"puts everything in his or her mouth."
- Complications:
    - Ingestion of paint chips can → lead poisoning.

WARD TIP

Pica is found commonly in PDD and schizophrenia.

- Hair or large objects can cause bezoar with bowel obstruction.
- Sharp objects such as pins or nails can cause intestinal perforation.
- Ingestion of feces or dirt can result in parasitic infections.

TREATMENT

- Often remits spontaneously.
- Treat underlying vitamin deficiency, if present.
- Psychotherapy—assess why pica is occurring.
- Behavior modification.
- Direct observation and removal of potential pica.

Somatic Symptom and Related Disorders

See Table 21-2 comparing somatoform disorders, factitious disorders, and malingering.

DEFINITION

- Somatic symptoms with significant distress or impairment in social, occupational, or other areas of functioning.
- Includes somatic symptom disorder, conversion disorder, pain disorder (functional neurological symptom disorder), illness anxiety disorder, factitious disorder, psychological factors affecting other medical conditions.

TREATMENT

- Psychodynamic therapy: Gain insight into unconscious conflicts and understand how psychological factors have influenced maintenance of the symptoms.
- Identify and **eliminate sources of secondary gain** in order to avoid reinforcing the symptoms.
- Improve self-esteem, promoting assertiveness, and teach non-somatic ways to express distress.
- Group therapy: Learn better coping strategies and improved social skills.

SOMATIC SYMPTOM DISORDER

- More than one somatic symptom that results in disruption of daily life.
- Symptomatic with any symptom for >6 months.
- Must meet two of the following criteria:
  - High health-related anxiety.
  - Disproportionate and persistent concerns about the medical seriousness of one's symptoms.
  - Excessive time and energy devoted to these symptoms or health concerns.

TABLE 21-2.   **Somatic Symptoms versus Factitious Disorders versus Malingering**

DISORDER	DEVELOPMENT OF SYMPTOMS	REASON FOR SYMPTOMS
Somatic symptoms	Unconscious	Unconscious
Factitious disorder	Conscious	Unconscious (primary gain)
Malingering	Conscious	Conscious (secondary gain)

- Symptoms do not necessarily have to be medically explained, but must be accompanied by excessive thoughts, feelings, behavior.
- Comorbidities: Depression, IBS, fibromyalgia, chronic pain, PTSD, history of sexual or physical abuse.

CONVERSION DISORDER

DIAGNOSIS

- Sensory symptoms, motor deficits, or pseudoseizures that are **not intentionally produced**.
- Cannot be explained by an organic etiology.
- Initiation of the symptom or deficit preceded by a psychological stressor.
- Unintentional and involuntary.
- Appropriate investigation leaves no medical explanation of symptoms.
- Symptoms cause impairment in social functioning.
- Other etiologies for the clinical presentation are ruled out.

ETIOLOGY

- Psychodynamic theory: Certain developmental predispositions respond to particular types of stress with conversion symptoms.
- Behaviorists: A learned excess or deficit that follows a particular event or psychological state and is reinforced by a particular event or set of conditions.
- Sociocultural: Predisposition of various ethnic and social groups to respond to stress with conversion symptoms.

EPIDEMIOLOGY

- Rare in children <10 years.
- Incidence ↑ in children who have experienced physical or sexual abuse and in those whose parents are seriously ill or have chronic pain.

SIGNS AND SYMPTOMS

- Paralysis, abnormal movements, inability to speak, see, hear; pseudoseizures.
- Usually occurs within the context of a primary illness such as major depression, schizophrenia, or somatization disorder.
- *La belle indifference*, the lack of interest in potentially life-altering symptoms, is common in adults, but rarely occurs in children.

Psychological Factors Affecting Other Medical Conditions

ANXIETY DISORDER

A 17-year-old girl becomes very concerned that a small lump in her left breast is "malignant cancer." Her histopathology report showed it to be entirely benign. Despite reassurance by her physician, you are now the fourth doctor she comes to for an additional opinion. She has hypochondriasis, preoccupied with a fear of a disease despite conclusive medical information, which is defined as a preoccupation with fears of having, or the belief that one has, a serious disease based on misinterpretation of bodily symptoms. The key feature in this condition is an abnormal concern that one is developing or has a serious illness. Psychotherapy that includes exploration of current life problems often result in symptom resolution.

DIAGNOSIS

- Preoccupation with having or fear of having a disease for >6 months.
- Somatic symptoms are mild or nonexistent.
- Persistent preoccupation despite adequate medical evaluation and assurance.
- Causes impairment in social functioning.
- Illness preoccupation cannot otherwise be explained by other mental disorders such as GAD.
- Other psychiatric diseases ruled out.

ETIOLOGY

- Associated with anxiety, depression, and narcissistic traits.
- Past experience with serious illness as a child or of a family member.

SIGNS AND SYMPTOMS

- Multiple visits to different doctors and deterioration of doctor–patient relationships.
- Individuals often believe that they are not receiving proper care so they pursue more opinions.
- Receive many evaluations and unnecessary surgeries.
- May become addicted to drugs as a result of their chronic ongoing physical complaints.

TREATMENT

- The primary aim of therapy is to help the patient identify and manage the fear of serious illness.
- In addition to techniques helpful for somatoform disorders:
  - Behavior modification techniques: Earn points to participate in daily routine despite feeling sick.
  - Educate about physiologic mechanisms.

> **EXAM TIP**
>
> Anxiety disorder can → strained social relationships because of preoccupation with perceived condition and the patient's expectation of receiving special treatment.

BODY DYSMORPHIC DISORDER

- Preoccupation with imagined defect in appearance or excessive concern about a slight physical anomaly (e.g., large nose, small muscles).
- Multiple visits to plastic surgeons or dermatologists are common.
- Typical age of onset 12–13, average age of onset 16–17.
- Risk factor: Child maltreatment such as abuse.
- Comorbidities: Depression, substance abuse, OCD.
- Treatment: Difficult to treat, CBT, SSRI, or combination has been effective.

Factitious Disorders

MUNCHAUSEN SYNDROME

DEFINITION

Intentional production or feigning of symptoms (e.g., thermometer manipulation, self-injury, ingestion, injection) **for primary gain** (e.g., relief of anxiety, assuming the sick role).

ETIOLOGY

- Children who make themselves sick may have been victims of Munchausen by proxy.
- Experience of misuse of illness to get attention and reinforcement of these actions.

TREATMENT

- Younger children are more likely than older children/adolescents to admit to deception if approached in a direct and concerned (not accusatory) way.
- Family therapy: Recognize how family communicates through illness and identify more effective ways of communication and getting what they need from family members.
- Involvement of primary care doctor/pediatrician in confrontation.

MUNCHAUSEN SYNDROME BY PROXY (MBP)

DEFINITION

- Intentional fabrication or actual production of symptoms in a child by a caregiver (usually the mother) in order to gain attention for themselves.
- A form of child abuse.

EPIDEMIOLOGY

- Adults who commit MBP may have a history of factitious disorders themselves.
- Ninety-eight percent of perpetrators are women. Most often offender is parent of child.
- Mortality rate is 9%.
- Up to 75% of the morbidity involved relates to physicians trying to treat the unknown conditions.

SIGNS AND SYMPTOMS

- Conditions that do not respond to treatment or whose courses are puzzling and persistent, often:
    - Vomiting/diarrhea (ingestion, syrup of ipecac).
    - Rashes (due to scrubbing with solvents).
    - Failure to thrive.
    - Seizures.
    - Infections.
    - Adding blood or other substances to urine specimens.
- Physical or laboratory findings that are unusual, discrepant, or clinically impossible or do not occur in the absence of the parent.
- Medically knowledgeable/fascinated mother who appears very connected to the hospital setting, who is reluctant to leave the child, and herself is dramatic and desires attention.
- Family history of similar problems or unexplained death in sibling.
- Signs or history of factitious disorder in mother.

TREATMENT

- Appropriate physician suspicion, good medical records, and reporting of abuse (often multiple doctors have been visited, with little continuity).
- Caregiver requires psychiatric therapy, such as for other factitious disorders.

WARD TIP

Malingering	Munchausen
Secondary gain (avoiding chores/school)	Primary gain (gain attention for self)

MALINGERING

DEFINITION

Intentional creation of symptoms for secondary gain (e.g., getting out of going to school or doing chores).

Personality Disorders

Patterns of behavior that deviate from cultural standards, can begin in adolescence or early adulthood. See Table 21-3.

- **Cluster A: "Weird"**
  - **Paranoid**: Distrustful and suspicious.
  - **Schizoid**: Wants to be isolated, a loner type with limited emotional expression.
- **Cluster B: "Wild"**
  - **Borderline**: Unstable mood, impulsive, splitting (a relationship is either awful or perfect).
  - **Histrionic**: Attention seeking (including seductive behavior), excessive emotionality (think soap operas).
  - **Narcissistic**: Demands the best, needs to be admired, entitled, lacks empathy.
  - **Antisocial**: Lacks remorse, violates laws of society, breaks the law (if <18 years = Conduct Disorder).
- **Cluster C: "Worried"**
  - **Obsessive-compulsive**: Find pleasure in completing ritualistic actions.
  - **Avoidant**: Wants relationships with others but intense fear of ridicule and being disliked.
  - **Dependent**: Needs to be taken care of, cannot be on their own, submissive.

TABLE 21-3.   **Personality Disorder Distinctions**

Disorder	Identifying Feature
OCPD	Find pleasure after completing actions
OCD	Feel distressed after actions
Avoidant	Wants relationships
Schizoid	Wants to be alone

NOTES

Pediatric Life Support

Pediatric Basic Life Support (BLS)

- The great majority of pediatric cardiopulmonary arrests outside the hospital setting occur with parents or their surrogates (i.e., teachers, coaches, day care workers, babysitters) nearby. BLS courses should be particularly targeted toward these individuals.
- Most cardiac arrests in children are caused by **progressive respiratory failure** and **circulatory collapse.**

EPIDEMIOLOGY

- Primary cardiac arrest is rather uncommon in children. It is most often **asphyxial,** resulting from respiratory failure or shock, or both.
- Outcomes are generally poor: Out-of-hospital setting 5–12% survival; in-hospital setting about 27% survival.
- The incidence of pediatric arrests is highest during infancy (age <1) but is lower among children and adolescents.
- Survival to discharge is more common among children and adolescents than infants or adults.
- During **infancy,** the leading causes of arrest are **injuries** (intentional and unintentional), **respiratory diseases, airway obstruction** (e.g., foreign body aspiration), **sepsis, drowning,** and **sudden infant death syndrome (SIDS).**
- During **childhood** and **adolescence,** the leading cause of arrest is **injury** (intentional and unintentional).
- **Injuries** should be viewed as **preventable** (not accidents), and education about injury prevention is an important aspect of pediatric BLS.

Fatal Pediatric Injuries

Most common causes of fatal pediatric injuries:
1. **Motor vehicle injuries:**
   - Nearly 50% of all pediatric injuries or deaths.
   - Risk factors include misuse of child seat restraints, seat belts, and airbags; adolescent drivers; and intoxicated drivers.
2. **Pedestrian injuries:** Leading cause of injury in ages 5–9.
3. **Bicycle injuries:** Helmets reduce morbidity of head and brain injuries by 85–90%.
4. **Drownings:**
   - Twenty percent of drowning victims who survive suffer permanent brain injury secondary to prolonged hypoxia.
   - Children younger than age 4 are at especially high risk.
   - Alcohol is often associated with adolescent drownings.
5. **Burns:**
   - Eighty percent of all fatalities occur from house fires (mostly from smoke inhalation).
   - Contact burns, electrical burns, and scaldings most often affect children below the age of 4.
   - Smoke detectors can reduce morbidity and mortality of house fires by 90%.
6. **Firearms:**
   - Second leading cause of death in all adolescent males and the leading cause of death in African-American adolescents.
   - Two-thirds of American households have firearms; one-third have a handgun.

Burns

- Upper extremities most frequent, followed by face and neck.
- Pediatric considerations:
    - Larger body surface area-to-body mass ratio.
    - Thinner skin = deeper burns.
    - ↑ fluid loss → greater fluid resuscitation requirement.
    - ↑ risk for hypothermia.

PATHOPHYSIOLOGY

Disruption of three functions of skin:
- Regulation of heat loss.
- Preservation of body fluids.
- Barrier to infection.

EPIDEMIOLOGY

- Third leading cause of accidental death in children.
- Occurs commonly in toddlers, due to their curious nature and lack of understanding of danger.
- Non-accidental burns estimated as high as 20% of all burn admissions.

CLASSIFICATION

Four criteria:
- **Depth:**
    - **Superficial thickness**: First degree (e.g., sunburn): Superficial. Only epidermis involved. Erythema, pain, and **absence of blisters,** generally heals within 1 week without scarring.
    - **Partial thickness:** Second degree, involved the epidermis and portions of the dermis.
        - Superficial partial thickness: Blister formation, painful, red, and weeping, and blanch with pressure, generally heals within 7–21 days, scarring is unusual.
        - Deep partial thickness: Extends deeper into the dermis, blister formation, damages hair follicles, painful to pressure only, does **not** blanch with pressure, generally heals within 3–9 weeks with hypertrophic scarring likely.
    - **Deep partial thickness:** Full thickness. Destroys epidermis and all of the dermis. **Painless, dry, and does not blanch.**
    - **Full thickness:** Third degree, destroys epidermis and all of the dermal layers leading to an eschar, no blisters, painless, dry, and does not blanch, appears waxy or leathery. Wound contractures are typical.
- **Percentage of body surface area:** A thorough and accurate assessment of burn size is essential to determine appropriate care.
    - Lund-Browder method: Most accurate, particularly in children (Figure 22-1).
    - Rule of nines: More expeditious method, but not accurate in children.
        - Each leg 18%.
        - Each arm 9%.
        - Front and back of trunk 18% each.
        - Head 9%.
    - Palm method: Good method for estimating small or patchy burns, palmar surface of the hand not including fingers is 0.5% and with fingers is 1%.

WARD TIP

Burns indicating abuse generally do not have a typical splash pattern. It is more linear with clear lines of demarcation or "stocking and glove" appearance (submersed in a hot bath).
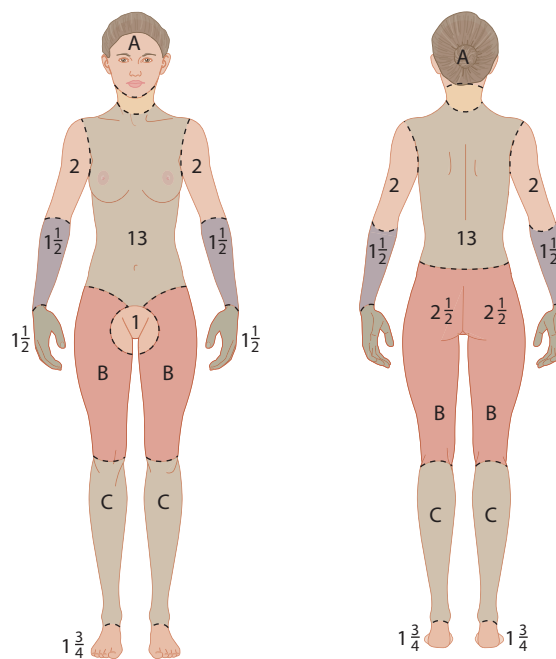
Relative percentages of areas affected by growth (age in years)

	0	1	5	10	15	Adult
A: half of head	$9\frac{1}{2}$	$8\frac{1}{2}$	$6\frac{1}{2}$	$5\frac{1}{2}$	$4\frac{1}{2}$	$3\frac{1}{2}$
B: half of thigh	$2\frac{3}{4}$	$3\frac{1}{4}$	4	$4\frac{1}{4}$	$4\frac{1}{2}$	$4\frac{3}{4}$
C: half of leg	$2\frac{1}{2}$	$2\frac{1}{2}$	$2\frac{3}{4}$	3	$3\frac{1}{4}$	$3\frac{1}{2}$

Second-degree _____ and

Third-degree _____ =

Total percent burned _____

F I G U R E   2 2 - 1 .   Lund-Browder diagram for estimation of burn size. (Reproduced, with permission, from Tintinalli JE, Stapczynski JS, Ma OJ, Yealy DM, Meckler GD, Cline DM. *Tintinalli's Emergency Medicine: A Comprehensive Study Guide*. 8th ed. New York: McGraw-Hill Education, 2016. Figure 216-3.)

- **Location:**
  - Assess risk for disability.
  - Worse on face, eyes, ears, feet, perineum, or hands, increased risk of poor cosmesis and contractures.
- **Association with other injuries.**

TREATMENT

- Airway, breathing, and circulation (**ABCs**) first!
  - **Airway:** Facial or neck burns, singed nose hair, **hoarseness,** or soot around mouth or nares may indicate inhalational injury. Assess for airway patency.
  - **Breathing:** Check arterial blood gases (ABGs) and check CO levels.
  - **Circulation:** IV fluid resuscitation.
- Infants: >10% of body surface area (BSA).
- Children: >15% BSA.
- IV/IO access and the Parkland formula:

$$\text{Parkland formula} = [\text{wt kg} \times \% \text{ burn} \times 4 \text{ mL/kg}]$$
$$+ \text{ maintenance fluid requirements}$$

Administer one-half over first 8 hours and remainder over next 16 hours.
- Superficial and partial thickness:
    - Rapid and effective analgesia.
    - Cold compresses.
    - Antiseptic cleansing.
    - Debride open blisters.
    - Topical antibiotic (silver sulfadiazine or bacitracin zinc ointment on the face).
    - Protect with bulky dressing.
    - Reexamine in 24 hours and serially after for healing and infection.
- Full thickness or extensive partial thickness:
    - ABCs of trauma, especially airway.
    - Fluid and electrolyte replacement (as above).
    - Sedation and analgesia is usually necessary.
    - Clean and manage as above.

CRITERIA FOR ADMISSION/TRANSFER

- Admit:
    - Two to five percent of full-thickness burn.
    - Five to ten percent of body surface.
- Other considerations for admission:
    - Burns involving the face, hands, genitalia, perineum, or major joints.
    - Circumferential extremity burns.
    - High-voltage electrical burns.
    - Significant chemical burns.
    - Inhalation injury.
    - Suspicion of abuse or unsafe home environment.
- Burn unit:
- >5% of full-thickness burn.
- >10% BSA.

BLS Algorithm

1. Determine unresponsiveness: Stimulate and check for responsiveness.
2. If unresponsive, shout for help (send someone to phone 911) and get automatic external defibrillator (AED). If lone provider: for **sudden collapse,** phone 911 and get AED. Assess for pulse, if no pulse start **C**hest compressions.
3. **A**irway (open): Head tilt–chin lift maneuver or jaw thrust maneuver (if cervical spine injury is suspected) after first set of compressions.
4. **B**reathing:
    - Provide two rescue breaths
        - **Infants** (<1-year-old): Place mouth over infant's mouth and nose, creating a seal.
        - **Children** (>1-year-old): Pinch nose and create mouth-to-mouth seal.
    - **Check pulse every 2 minutes.** If no pulse, continue with cycles.

> **WARD TIP**
>
> **BLS:** Determine unresponsiveness, call for help, and remember your **CABs:**
> **C**hest Compressions
> **A**irway
> **B**reathing

INFANT COMPRESSIONS

For <1 year of age:
- **Single provider:**
    - Place one hand on the head to maintain open airway for ventilation.
    - Place the two middle fingers of the other hand on the sternum one fingerbreadth below the nipple line to be used for chest compressions.

- Chest compressions of 1.5 inch in depth at a rate of *at least* 100 per minute.
- Coordinate compressions with pauses for ventilation at a ratio of 30:2.
- **Two providers:**
    - Use hands encircling chest method with thumbs on sternum for chest compression.
    - Compression to ventilation ratio is 15:2.
- If collapse is unwitnessed, 2 minutes of BLS are provided to children before activating the Emergency Medical Services (EMS) system, because most cardiopulmonary arrest in children is caused by the development of hypoxemia, and ventilatory and circulatory support may delay or prevent the development of cardiac arrest.

CHILD COMPRESSIONS

Chest compressions should be initiated if heart rate is <60 beats/min. For child age 1 to puberty:
- Place one hand on the head to maintain open airway for ventilation.
- Place the heel of the other hand on the lower half of the sternum (take care to avoid the xiphoid).
- Chest compressions of 2 inches in depth at a rate of 100 per minute.
- Coordinate compressions with pauses for ventilation at a ratio of 30:2 for single provider and 15:2 for two providers.
- High-quality cardiopulmonary resuscitation (CPR):
    - Push hard and fast (at least 100/min).
    - Release completely (allow for full chest recoil).
    - Minimize interruptions during compressions (<10 seconds).

FOREIGN BODY AIRWAY OBSTRUCTION

A 2-year-old boy is found unresponsive on the floor of his bedroom. He was last seen by his mother playing with building blocks. She states she only left the child alone for a few minutes while she went to use the bathroom. When EMS arrives, they find a cyanotic infant, unresponsive, not breathing. Pulses are palpable with a heart rate of 137. What are the initial and critical actions that must be taken?

In this case, foreign body aspiration is highly suspicious. This patient is unconscious, so a Heimlich maneuver should not be attempted. The victim should be placed supine, then the airway is opened with head-tilt chin-lift; *if you see the object,* attempt a finger sweep to remove it. Attempt rescue breathing. If unsuccessful, reposition head and attempt rescue breathing. If still unsuccessful, straddle the victim, placing the heel of one hand on the child's abdomen in the midline just above the umbilicus (avoiding the xiphoid). Place the other hand on top of the first and deliver five quick inward and upward thrusts. Repeat this maneuver until ventilation is successful.

- Foreign body airway obstruction should be considered in any child who suddenly demonstrates signs of respiratory distress, gagging, coughing, wheezing, or stridor.
- These symptoms of airway obstruction can also be caused by infection. Infectious etiologies of airway obstruction are pediatric emergencies and should be suspected if fever, congestion, hoarseness, drooling, lethargy, or atony is present.
- If an infectious cause of airway obstruction is being entertained, the child must be transported immediately to the nearest hospital capable of emergent pediatric intubation.

- **Infant compressions:** Hands encircling chest 1.5-inch depth or at least one-third of AP chest diameter, rate >100/min, 15:2 ratio (two providers).
- **Child compressions:** Heel of palm 2-inch depth or at least one-third of AP chest diameter, rate 100/min, 15:2 ratio (two providers).

INFANT AIRWAY OBSTRUCTION (<1 YEAR OF AGE)

Back blows and chest thrusts:
1. Activate EMS.
2. Hold the choking infant in one arm, with the infant face down, firmly holding the jaw and allowing the body to rest on your forearm.
3. Deliver five **back blows** using the heel of your free hand directly between the infant's shoulder blades.
4. If no improvement, turn the infant over to the face-up position, maintaining support of the head and neck.
5. Deliver five quick **chest thrusts** using the same technique as for infant chest compressions.
6. Repeat above steps, alternating back blows and chest thrusts, until object is removed or the child loses consciousness.

CHILD AIRWAY OBSTRUCTION (>1 YEAR OF AGE)

- Heimlich maneuver—if **conscious:**
  1. Ask patient if she is choking and if she can speak.
  2. If not, tell patient you are going to help her and activate EMS.
  3. Stand behind the conscious victim, and wrap your arms around the abdomen.
  4. Place the thumb of one fist in the midline of the abdomen just above the umbilicus (well below the xiphoid).
  5. Grasp the fist with the other hand and deliver quick thrusts inward and upward.
  6. Continue until object is expelled or victim becomes unconscious.
- If the victim becomes **unconscious** (witnessed):
  1. Place victim supine.
  2. Open the airway with head-tilt chin-lift; *if you see the object*, attempt a finger sweep to remove it.
  3. Attempt rescue breathing.
  4. If unsuccessful, reposition head and attempt rescue breathing.
  5. If still unsuccessful, straddle the victim, placing the heel of one hand on the child's abdomen in the midline just above the umbilicus (avoiding the xiphoid).
  6. Place the other hand on top of the first and deliver five quick inward and upward thrusts.
  7. Repeat steps 2–6 until ventilation is successful or EMS arrives and takes over.

Pediatric Advanced Life Support (PALS)

- Goals: To provide rapid assessment and definitive management of the pediatric arrest situation using advanced airway management techniques, cardiac monitoring equipment, and pharmacologic therapy.
- Respiratory problems are rather common among children, and respiratory arrest is the major cause of cardiac arrest in the pediatric population.

EXAM TIP

Most common cause of foreign body airway obstructions in children are balloons, small objects (toys), and food (hot dogs, nuts, grapes, round candy).

EXAM TIP

Ninety percent of foreign body deaths are in children under age 5; two-thirds of these are infants.

WARD TIP

Airway obstruction caused by infection requires immediate transport to the hospital.

WARD TIP

Infant airway obstruction = 5 back blows + 5 chest thrusts.

WARD TIP

Child (>1 year of age) airway obstruction = Heimlich maneuver.

- If respiratory arrest is treated before it progresses to cardiac arrest, survival is markedly improved.
- If respiratory arrest progresses to pulseless cardiac arrest, the chances of survival are poor.
- Early recognition of respiratory failure and effective management of respiratory problems are key elements taught in PALS.

ANATOMIC DIFFERENCES IN THE PEDIATRIC AIRWAY

- Infants are obligate nasal breathers.
- Smaller airway.
- Tongue occupies a greater percentage of the oropharynx.
- Vocal cords are more superior and anterior.
- The tonsils and adenoids are more prominent.
- The epiglottis is larger and more floppy.
- The tracheal rings are less rigid.
- The narrowest part of the airway is just below the vocal cords at the non-distensible **cricoid** cartilage; endotracheal tube (ETT) size is thus determined by the size of this opening.
- Smaller amounts of vocal cord edema can drastically reduce the diameter of the airway (resistance is inversely proportional to the fourth power of the radius).
- The angle between the base of the tongue and the glottis is more acute.

PEDIATRIC RESPIRATORY DISTRESS

- The *earlier* you detect respiratory distress or respiratory failure and start the appropriate therapy, the better chance the child has for a *good* outcome.
- Respiratory distress → hypoxemia (inadequate oxygenation) and/or hypercarbia.

$$\text{Arterial oxygen content} = (1.36 \times \text{Hgb concentration} \times \text{SaO}_2) + (0.003 \times \text{PaO}_2)$$

- Hypoxemia is readily detected noninvasively with pulse oximetry monitoring.
- Hypercarbia results from inadequate alveolar ventilation (i.e., ↑ CO_2 tension ($PaCO_2$) in the blood).
- Provide oxygen in the highest concentration available to any child experiencing respiratory difficulty (face tent, blow-by stream, mask, partial nonrebreather).
- Suction secretions as needed (don't forget the nose in infants).
- Continually reassess for signs of decompensation; if a trend of worsening respiratory status is noted, assisted ventilation is required to prevent respiratory failure.
- Upper airway obstruction: Predominantly during **inspiration:**
    - Tachypnea.
    - Retractions.
    - **Stridor:** Classic sign of upper airway obstruction.
- Lower airway obstruction: Signs of obstruction:
    - Tachypnea.
    - **Wheezing:** Most common, generally expiratory.

EXAM TIP

Poiseuille's equation:
Resistance (airway) × $1/r^4$

WARD TIP

Straight laryngoscope blades are more effective to visualize the pediatric airway. Used to "pick up" epiglottis.

WARD TIP

In general, respiratory rates <10/min or >60/min are always abnormal.

MANAGEMENT OF RESPIRATORY FAILURE AND PEDIATRIC INTUBATION

Timing is everything! If respiratory function is restored promptly, neurologically intact survival is likely:

- **A**irway: Open the airway.
- **B**reathing: Support breathing using bag-valve-mask ventilation until definitive airway is established (i.e., endotracheal intubation). Monitor oxygenation and end tidal CO_2 (after intubation).
- **C**irculation: Assess circulation, establish intravenous (IV) access, chest compressions if necessary.

ENDOTRACHEAL INTUBATION

- Endotracheal tube size: For children 1–10 years:
  - Uncuffed endotracheal tube size (mm ID) = (age in years/4) + 4.
  - Cuffed endotracheal tube size (mm ID) = (age in years/4) + 3.
- Cuffed tubes are generally safe and preferred for use in the hospital setting.
- Keep cuff inflation pressure <20 cm H_2O.
- Select and prepare all equipment prior to attempting intubation (make sure all are functioning well).
- Laryngoscope blade (Figure 22-2): Size:
  - Infant: Miller (straight) 0.
  - Age <1: Miller (straight) 1.
  - Age 1–5: Miller (straight) 2.
  - Age >5: Mac (curved) 2 or Miller 2–3.
  - Age >12: Mac (curved) 3–4 or Miller 3–4.
- ETT size: Based on above formulas.
- Confirm placement with end-tidal CO_2 indicator.
- Listen in both lung fields for equal breath sounds and confirm absent gastric insufflation.
- If the intubated patient's condition deteriorates, consider the following possibilities (**DOPE**):
  - **D**isplacement of the tube from the trachea.
  - **O**bstruction of the tube.
  - **P**neumothorax.
  - **E**quipment failure.

VASCULAR ACCESS

Cannulation of Peripheral Veins

- **Upper extremity:**
  - Median cubital vein.
  - Cephalic vein (and tributaries in the dorsum of the hand).
  - Basilic vein.
- **Lower extremity:**
  - Saphenous veins (especially great saphenous at the ankle).
  - Veins of the dorsal arch.
  - Median marginal veins.

Intraosseous Cannulation

- Rapid and reliable method to deliver fluids and drugs during resuscitation.
- Preferred over ET route for the administration of drugs.
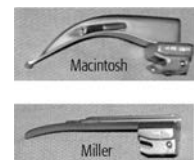
FIGURE 22-2. Two common types of laryngoscope blades: Macintosh and Miller blades. (Reproduced, with permission, from Lalwani AK. *Current Diagnosis & Treatment in Otolaryngology—Head & Neck Surgery.* New York: McGraw-Hill, 2004: 1700).

WARD TIP

More than just ETT size!
  ET tube size: (Age in years/4) + 3
  Foley and Suction Catheter size: 2× ETT size
  Length at teeth of ETT placement: 3× ETT size
  Chest tube size: 4× ETT size

WARD TIP

Unpredictable drug absorption when drug administration via the ETT.

WARD TIP

LEAN: Lidocaine, epinephrine, atropine, and naloxone (can be administered via ET route if vascular access is not available).

- Temporary route (limit 24 hours).
- Contraindications:
    - Open fracture at proposed insertion site.
    - Signs of skin infection at the insertion site.
    - Previous attempts at site.
- During cardiopulmonary resuscitation (CPR), should be employed after three failed attempts to cannulate peripheral veins (or 90 seconds).
- Preferred site of insertion:
    - Proximal tibia: Two fingerbreadths below the tibial tuberosity.
    - Remember to insert needle at an angle pointing **away** from the growth plates.
- Can safely administer fluids, blood products, and drugs. (Anything that can be given via central line can be given by intraosseous route.)

COMPLICATIONS

- Rare (<1%).
- Extravasation → compartment syndrome.
- Infections → cellulitis and osteomyelitis.
- Fractures.
- Injury to the epiphyseal growth plate.

Cannulation of Central Veins

- Complications (bleeding, infection, pneumothorax, etc.) are more common in the pediatric age group.
- Central catheters should be used only when the benefit outweighs the risks (i.e., when central venous pressures need to be monitored).
- Catheters are inserted using the Seldinger (guidewire) technique.
- Common sites include:
    - Femoral vein.
    - Internal jugular vein.
    - Subclavian vein.

SHOCK AND FLUID RESUSCITATION

- Shock is defined as inadequate oxygen delivery to the tissues and organs.
- Shock can result from:
    - Inadequate blood volume or oxygen-carrying capacity (e.g., hypovolemic/hemorrhagic shock).
    - Inappropriately distributed blood volume (distributive shock).
    - Impairment of heart contractility (cardiogenic shock).
    - Obstructive blood flow (obstructive shock).
- All forms of shock require consideration of fluid administration during initial therapy.
- **Septic shock, neurogenic shock,** and **anaphylactic shock** are all characterized by vasodilation, ↑ capillary permeability, and third-space fluid loss that results in an intravascular hypovolemia. These are subcategories of distributive shock.
- **Cardiogenic shock** may even require initial fluid administration before the initiation of inotropic and chronotropic agents ("you must fill the tank before starting the engine"). Judicious use of fluids mandatory to avoid causing pulmonary edema.
- The treatment goal for shock is to prevent end-organ injury and halt the progression to cardiopulmonary failure and cardiac arrest.
- Initial fluid resuscitation:
    - Normal saline or lactated.
    - Ringer's (isotonic).

Administration of Fluid Bolus

- Initial bolus should be a rapid infusion of isotonic crystalloid of 20 mL/kg over 20 minutes.
- Reassess after initial bolus by looking at response in heart rate, capillary refill, level of consciousness, and most importantly *urinary output.* Aim for a urinary output of 0.5–1 cc/kg/hr.
- **Blood** is the preferred fluid replacement for trauma victims demonstrating persistent hypovolemic shock *after* two to three boluses of crystalloid (i.e., 40–60 mL/kg).
- Maintenance fluids are given by the 4,2,1 formula: 4 mL/kg/hr for the first 10 kg + 2 mL/kg/hr for the second 10 kg + 1 mL/kg/hr for every 1 kg above 20.

Classification of Shock (Hemorrhagic/Hypovolemic Shock)

Class I
- 0–15% volume loss.
- Normal pulse.
- Normal blood pressure.
- Normal capillary refill.
- Normal respiratory rate.
- Urine output 1–2 mL/kg/hr.

Class II
- 15–30% volume loss.
- Mild tachycardia.
- Mildly ↓ blood pressure.
- Mildly prolonged capillary refill.
- Mild tachypnea.
- Urine output 0.5–1.0 mL/kg/hr.

Class III
- 30–40% volume loss.
- Tachycardia.
- ↓ blood pressure.
- Prolonged capillary refill.
- Tachypnea.
- Urine output 0.25–0.5 mL/kg/hr.

Class IV
- >40% volume loss.
- Severely tachycardic, bradycardic, or absent pulse.
- Very low blood pressure.
- Greatly prolonged capillary refill.
- Severe tachypnea.
- Urine output 0 mL/kg/hr.

Pressor Support in Pediatric Shock

- First, attempt multiple fluid boluses.
- Try to identify and treat the underlying cause.
- Choose pressor agent according to the type of shock present.

Pharmacologic Agents Used in the Treatment of Shock

- Inotropes:
    - Dopamine.
    - Epinephrine.
    - Dobutamine.

EXAM TIP

Remember that only about 25% of crystalloid will remain in the intravascular space; thus, you may need to administer three times the estimated fluid loss (3:1 rule).

WARD TIP

Cold Shock: Cool extremities, delayed capillary refill
Warm Shock: Warm extremities, flash capillary refill

- Phosphodiesterase inhibitors:
  - Milrinone.
  - Inamrinone.
- Vasodilators:
  - Nitroglycerine.
  - Nitroprusside.
- Vasopressors:
  - Epinephrine.
  - Norepinephrine.
  - Dopamine.
  - Vasopressin.

Hypovolemic Shock

Multiple crystalloid boluses will be necessary (20 mL/kg bolus over 20 minutes, repeat PRN).

Septic Shock

Multiple crystalloid boluses will be necessary (20 mL/kg bolus over 5–20 minutes, repeat PRN).
- Consider dopamine 5–20 µg/kg/min if patient is **normotensive.**
- Consider epinephrine 0.1–1.0 µg/kg/min if patient is **hypotensive and in cold shock.**
- Consider norepinephrine 0.1–2.0 µg/kg/min if patient is **hypotensive and in warm shock.**

Cardiogenic Shock

- Initial fluid bolus is usually necessary.
- Consider dobutamine 5–20 µg/kg/min if patient is **normotensive.** (*Note:* Dobutamine may not be effective in infants and young children due to lack of stroke volume response.)
- Consider epinephrine 0.1–1.0 µg/kg/min if the patient is **hypotensive.**

CARDIAC ARRHYTHMIAS

- Tachycardias.
- Bradycardias.
- No pulse: Asystole, pulseless electrical activity (PEA), ventricular fibrillation (VF), or pulseless ventricular tachycardia (VT).

Tachyarrhythmias

Sinus Tachycardia
- Defined as a rate of sinus node discharge faster than normal for age.
- Typically, a response to a **need for ↑ cardiac output** (compensatory tachycardia).
- Common causes include fever, pain, anxiety, blood loss, sepsis, and shock.
- Always assess and **reassess ABCs.**
- Therapy entails treating the underlying cause.

Supraventricular Tachycardia (SVT)
- SVT is **rapid, very regular,** often **paroxysmal.**
- Often exceeds 220 bpm in infants, exceeds 180 bpm in children.
- P waves are absent or indistinguishable.
- QRS complex is typically narrow (<0.08 seconds).
- SVT is most commonly caused by reentry mechanism.

- **SVT algorithm:**
  - Assess ABCs, support as needed.
  - Administer 100% oxygen, ventilate as needed.
  - Document electrocardiogram (ECG)/rhythm tracing: Evaluate QRS—narrow ≤0.09 seconds.
  - Establish IV or IO access:
    - Adenosine 0.1 mg/kg rapid intravenous push, immediately followed by 5 mL of saline flush (maximum dose: 6 mg in children and 12 mg in adolescents).
    - Synchronized cardioversion if unstable: 0.5 to 1 J/kg; if not effective ↑ to 2 J/kg (sedate if possible, but do not delay cardioversion).
  - If still in SVT: Obtain cardiology consult and consider administration of:
    - Amiodarone 5 mg/kg IV over 20–60 minutes *or*
    - Procainamide 15 mg/kg IV over 30–60 minutes. If patient becomes unstable at any time, proceed directly with synchronized cardioversion.
- Management of SVT:
  - Stable: Vagal maneuvers and/or adenosine.
  - Unstable: Synchronized cardioversion.

Ventricular Tachycardia (VT) (with pulse)

- Wide QRS complex (>0.09 seconds).
- P waves not present.
- Very uncommon in children.
- Risk factors include prolonged QT syndrome, cardiac anomalies, drug ingestions, electrolyte abnormalities, underlying cardiac disease.
- **VT algorithm:**
  1. Assess ABCs, support as needed.
  2. Administer 100% oxygen, ventilate as needed.
  3. Document electrocardiogram (ECG)/rhythm tracing (*wide* QRS > 0.09 seconds).
  4. Establish IV or IO access or
  5. Synchronized cardioversion: 0.5–1 J/kg; if not effective, ↑ to 2 J/kg (sedate if possible, but do not delay cardioversion).
  6. If still in VT: Call cardiology consult for administration of:
     - Amiodarone 5 mg/kg IV over 20–60 minutes *or*
     - Procainamide 15 mg/kg IV over 30–60 minutes.
  7. Obtain cardiology consult as needed.
  8. Identify and treat possible causes:
     - **4Hs: H**ypovolemia, **H**ypoxemia, **H**ypothermia, **H**yper/hypokalemia.
     - **4Ts: T**amponade, **T**ension pneumothorax, **T**oxins, **T**hromboembolism.

Bradyarrhythmias

Bradycardia Algorithm

1. Assess ABCs, support.
2. Administer 100% oxygen, ventilate, prepare to intubate.
3. Establish IV/IO access.
4. Cardiac monitor, pulse oximetry, blood pressure cuff.
5. Reassess ABCs.
   - If stable, continue to support ABCs, admit for observation.
   - If unstable (poor perfusion, hypotension, heart rate <60, continued hypoxia despite 100% oxygen administration):
     1. Begin chest compressions if still persistent bradycardia.
     2. Give epinephrine 0.01 mg/kg (1:10,000, 0.1 mL/kg) IV/IO, or via ETT 0.1 mg/kg (1:1,000, 0.1 mL/kg). Repeat every 3–5 minutes.

WARD TIP

Ventricular tachycardia:
- QRS wide
- No P waves
- Rare in children

WARD TIP

Age-specific heart rates for bradycardia:
- 0–3 months (85–205 beats/min); bradycardia <85.
- 3 months–2 years (100–190 beats/min); bradycardia <100.
- 2–10 years (60–140 beats/min); bradycardia <60.
- >10 years (60–100 beats/min); bradycardia <60.

3. If ↑ vagal tone or primary AV block, give atropine 0.02 mg/kg IVP. Minimum dose: 0.1 mg. Max dose: 0.02 mg/kg to maximum of 1.0 mg via ETT dose: Two to three times dose in 5-mL normal saline.
4. Consider external pacing.

Pulseless Arrhythmias

> A 6-year-old girl with a past medical history of asthma is brought to your ED by EMS in respiratory distress. Her vital signs are heart rate 120, BP 90/50, RR 26, O_2 93% on facemask. Per EMS, the child had been wheezing all morning, and the mother had tried several nebulizer treatments without relief. The mother called 911 when her child seemed to become in more distress. While performing your primary survey the patient becomes unresponsive, the monitor shows v-fib. What are the initial and critical actions that must be taken?
> Here the patient is going into cardiac failure/arrest secondary to respiratory distress. The first step is to palpate for a pulse. This patient has ventricular fibrillation, which is a shockable rhythm.

Ventricular Fibrillation (VF)/Pulseless VT
1. Start chest compressions immediately.
2. Defibrillate as soon as possible × 1 with 2 J/kg.
3. Restart CPR for 2 minutes.
4. IV/IO access (do not delay defibrillation for access).
5. Give another shock, 4 J/kg; give epinephrine 0.01 mg/kg (0.1 mL/kg of 1:10,000) IV/IO or ETT 0.1 mg/kg (0.1 mL/kg of 1:1000).
6. Restart CPR for 2 minutes.
7. Give another shock 4 J/kg; consider giving antiarrhythmics: Amiodarone 5 mg/kg bolus IV/IO.
8. Consider magnesium 25 to 50 mg/kg IV/IO for Torsades de pointes (maximum dose: 2 g).
9. Identify and treat possible causes (4Hs and 4Ts).

Pulseless Electrical Activity (PEA)
- PEA in children, while rare, usually occurs as a result of **progressive respiratory and/or circulatory failure.**
- As with adult PEA, the **differential diagnosis** for pediatric PEA is essential to successful resuscitation.
- **PEA algorithm:**
  1. Start CPR.
  2. IV/IO access.
  3. Consider possible causes of PEA (and specific treatments):
     - Hypovolemia (volume—normal saline infusion).
     - Hypoxia (oxygen, intubation, ventilation).
     - Hypothermia (warmed normal saline infusion).
     - Massive pulmonary embolism (heparin infusion, thrombolysis).
     - Acidosis (sodium bicarbonate).
     - Tension pneumothorax (needle decompression).
     - Cardiac tamponade (pericardiocentesis).
     - Hyperkalemia (insulin/glucose, calcium).
     - Drug overdose from TCAs, digoxin, β-blockers, calcium-channel blockers.
  4. Epinephrine (every 3–5 minutes):
     - IV/IO 0.01 mg/kg (0.1 mL/kg of 1:10,000).
     - ETT 0.1 mg/kg (0.1 mL/kg of 1:1000).

Asystole

- Most common pulseless rhythm in children.
- Airway management and hyperventilation are the most important interventions.
- Always confirm asystole in more than one lead and ensure that leads are properly connected.
- **Asystole algorithm:**
  1. Start CPR.
  2. IV/IO access.
  3. Epinephrine (every 3–5 minutes):
     - IV/IO 0.01 mg/kg (0.1 mL/kg of 1:10,000).
     - ETT 0.1 mg/kg (0.1 mL/kg of 1:1000).
  4. Search for reversible causes.
- Note that atropine and bicarbonate are **not** part of the algorithm for asystole.

Neonatal Resuscitation

- Newborn resuscitation ideally should be performed in the delivery room, neonatal intensive care unit (NICU), or other unit with personnel experienced with treating newborns and equipment appropriate for the task.
- Birth asphyxia accounts for about 19% of the approximately 5 million neonatal deaths that occur each year worldwide.
- Approximately 10% of newborns require some assistance to begin breathing at birth; about 1% need extensive resuscitative measures to survive.

PREASSESSMENT AND TRIAGE

Always ask the following questions when treating a new born baby:

1. Was the baby born at term (i.e., how many weeks' gestation)?
   - Premature babies are at higher risk for intubation and resuscitation, especially if their respiratory system is not fully developed and functional.
2. Is there good muscle tone?
   - Healthy babies should have flexed extremities and be active.
3. Is the baby breathing or crying?
   - *Note*: Gasping usually indicates a significant problem and requires the same intervention as no respiratory efforts at all (apnea).

If the answer is "no" to any of these questions, newborn requires resuscitation care.

NEWBORN ASSESSMENT

- **Temperature:** Neonatal hypothermia can be associated with neonatal respiratory depression. Upon delivery, warming and drying with a towel or blanket is often adequate to stimulate breathing in a newborn.
- **Airway:** Position the airway and suction any secretions (neck slightly extended in the "sniffing" position).
- **Breathing:** Observe chest rise and fall, give 100% oxygen if necessary (but start with 21% oxygen), initiate adequate bag-valve-mask ventilation if necessary (i.e., heart rate <100 beats/min and unresponsiveness; absent or depressed respirations).

WARD TIP

Suction newborn airway gently and only when necessary.

WARD TIP

Effective ventilation is the most important factor in neonatal resuscitation.

- **Circulation:** Assess heart rate and color, provide chest compressions as necessary (if heart rate absent, if heart rate <60 despite 30 seconds of assisted ventilation).

NEWBORN RESUSCITATION

Assess every newborn (and give the appropriate support).
1. ABCs—assess and support.
   - **A**irway (position and suction).
   - **B**reathing (stimulate to cry).
   - **C**irculation (heart rate and color).
   - Temperature (warm and dry).
2. Oxygen.
3. Establish effective ventilation:
   - Bag-valve-mask.
   - Laryngeal mask airway (LMA) can be an effective alternative for establishing an airway when bag-valve-mask fails.
   - Endotracheal intubation (only by trained rescuer competent in neonatal intubations).
4. Chest compressions if pulse <60 beats/min, despite 30 seconds of effective positive-pressure ventilation. Place two hands around infant's chest with thumbs on sternum in the nipple line. Compress to one-third the anterior-posterior diameter.
5. Medications as dictated by the situation.

MECONIUM DELIVERIES

1. If the infant is active and vigorous, simply use a bulb syringe to suction mouth and nose gently.
2. If any signs of distress (absent or depressed respirations, heart rate <100, poor muscle tone), newborn needs full resuscitation measures.
3. If no improvement, start with bag-valve-mask ventilation and proceed with algorithm.
4. Routine direct tracheal suctioning either following endotracheal intubation or by using ETT as suction catheter is no longer recommended.

APGAR

See Gestation and Birth chapter.

Index

NOTES

NOTES

NOTES

NOTES

NOTES

NOTES